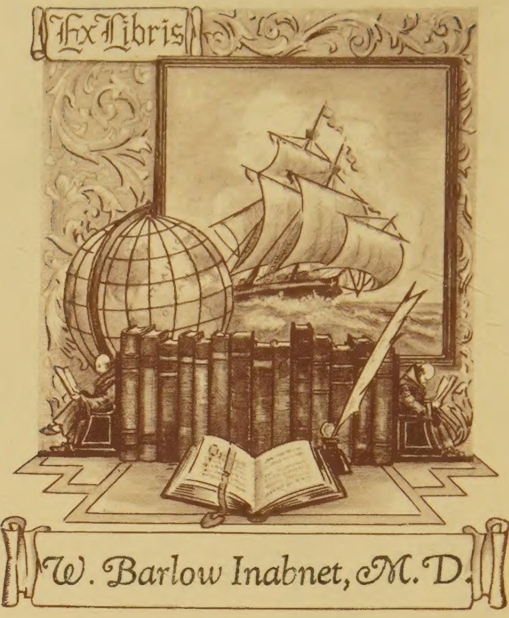
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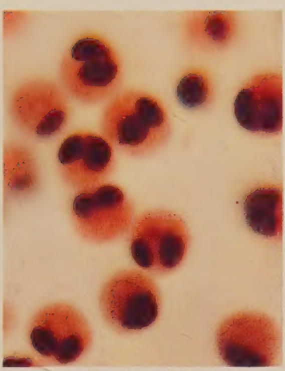
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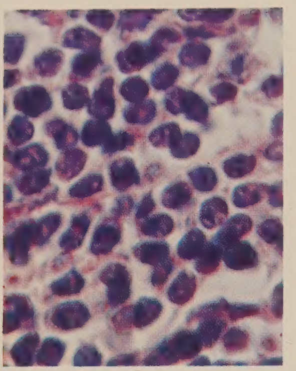
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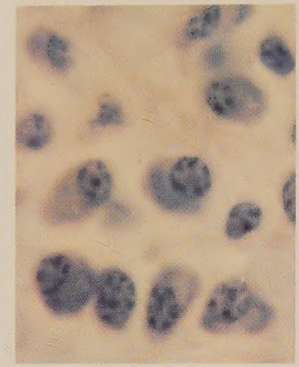
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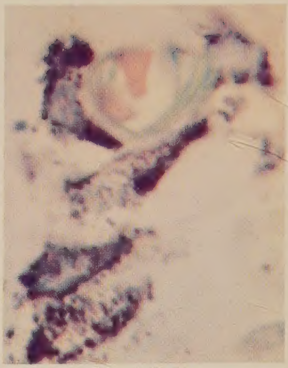
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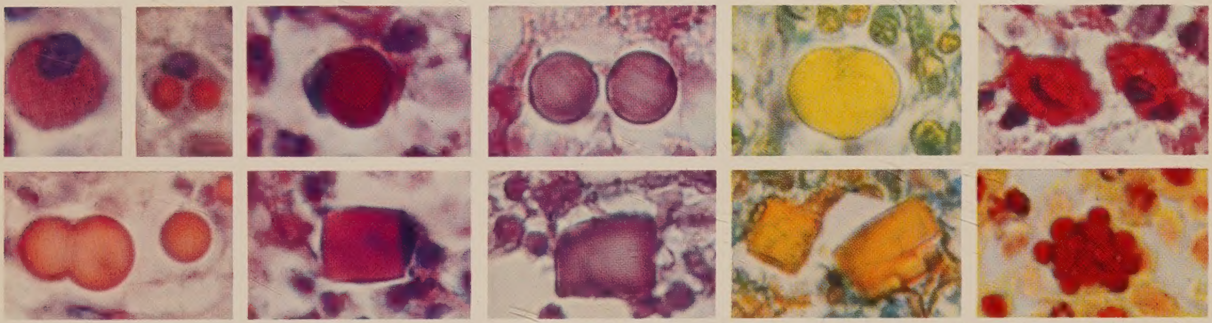
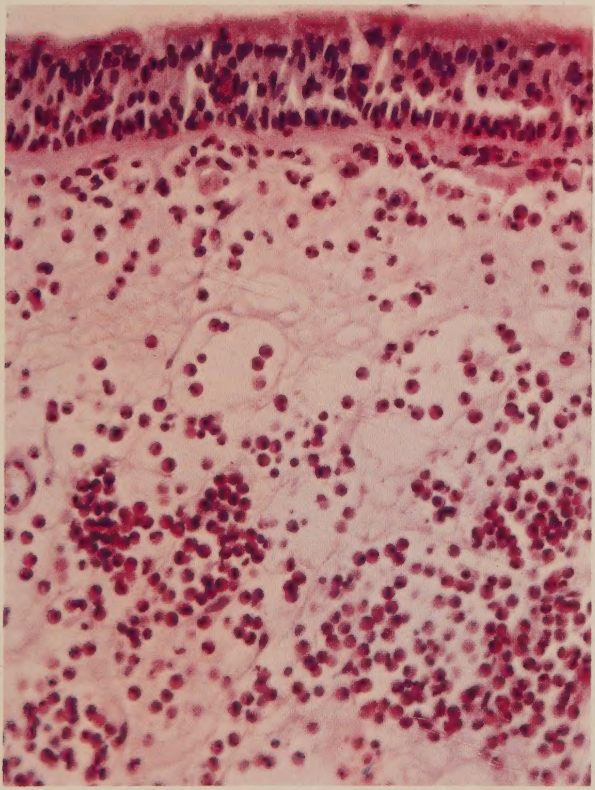
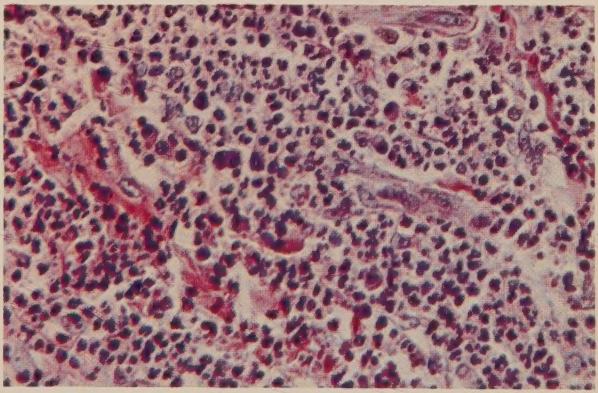
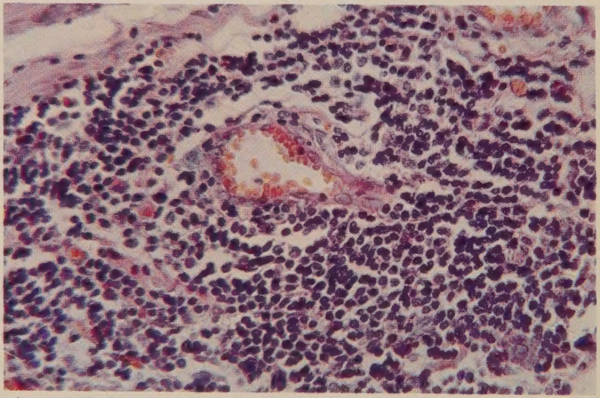

Hematoxylin-Eosin Hotchkiss-McManus Crystal Violet Acid Mucopolysaccharide Masson Trichrome

Russell Bodies. Some stages in development and various morphologic forms. (All about x1000).


Polypoid rhinitis, probably allergic. Edematous interstitial tissue, striking infiltration of eosinophils, and prominent basement membrane. x310.


Acute inflammation (upper). Neutrophilic leukocytes predominant cellular component. x285.


Chronic inflammation (lower) with lymphocytic cellular exudate. x 285.

AN ATLAS
of
OTOLARYNGIC PATHOLOGY

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FOREWORD

This Atlas of Otolaryngic Pathology is a concrete demonstration of the value of a registry of pathology. The contents are the result of years of selection and preparation on the part of the authors. But it is only through the contributions of otolaryngologists everywhere that they could draw on the wealth of material gathered together in the files of the Armed Forces Institute of Pathology. This volume is also a tribute to the foresight of the American Academy of Ophthalmology and Otolaryngology, which more than thirty years ago assumed leadership in advocating the importance of pathology to the clinician. We are gratified that we have been in a position to cooperate with this outstanding group and especially to have stimulated and participated in the production of this work. It is my firm belief that this is an achievement of which both the American Academy of Ophthalmology and Otolaryngology and the Armed Forces Institute of Pathology can well be proud.

ELBERT DE COURSEY
Brigadier General, U.S.A., M.C.
Director, Armed Forces Institute of Pathology.

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INTRODUCTION

Occasionally, a combination of skill and opportunity impels the production of what can be called a "classic." I believe that this Atlas on histopathology of the ear, nose and throat will be considered such a book. Never between two covers has so much basic pathology of the head and neck been compressed. As is usual from the Armed Forces Institute of Pathology, there is much new material because of the wealth of pathologic specimens from which to choose. There are so many photographs representative of each disease that a trained physician will often be able to diagnose his own material by studying its similarities to the illustrations. The old atlases were good; this one is magnificent. The material in it is the foundation for sound clinical judgment and advance in all branches of medicine as well as surgery of the head, the neck and the thorax.

Strangely enough, there are some who must underestimate the importance of microscopic pathology in the basic understanding of disease, for occasionally one hears remarks to the effect that this subject is overemphasized in the medical schools and even more by examining boards. There are those who speak of a more dynamic approach. Critics often emphasize the artificiality of the technique and point out its limitations.

Let us consider the limitations of micropathology, for, of course, there are some. One must have a well-equipped laboratory and highly trained technicians to prepare the specimens. Next, one must have skilled pathologists to interpret them. Perhaps, this is on the debit side, but it is no argument against histopathology *per se*. Skilled interpretation is necessary for all diagnostic modalities. As a matter of fact, histopathologic methods are far less subject to interpretive error than most other diagnostic procedures.

Since the slides themselves constitute a permanent record, the interpretations can be checked, not only immediately, but even in the distant future. Histopathology gives so accurate and useful a record that no conscientious surgeon can practice without it. He uses it to control and study his procedures, and it helps to temper over-enthusiasm, as well.

It is in the production of clear-cut, typical pictures in many magnifications that in most branches of medicine histopathology has done more than any other specialized technique to make the fundamentals of disease comprehensible. One of the reasons that diseases of the ear and nose are poorly understood is that routine pathologic material on the temporal bone and the sinuses is difficult and expensive to obtain and process. Therefore, it has not been done in most laboratories. Imagine if the kidneys or the lungs had been so neglected. No wonder we know nothing about the "common cold"!

The preparation used in micropathology is usually stained and passed through several chemicals. This manifestly changes the tissue from its living state. But to object to the artificiality of the technique used is like objecting to the written word. Prose, too, is artificial, but if skillfully written certainly contributes to a better understanding of what it depicts.

Let us seek further for more and better histologic techniques rather than deprecating those in current use. The ear, nose and throat are particularly suited for comparison of early and comparatively mild symptoms with the anatomic changes that can be seen with a microscope. The ear, nose, throat, bronchi and esophagus are comparatively accessible for biopsy studies. The modern otolaryngologist, with his skill in diagnosis, his ability to study cavities through a "keyhole," and his training in observation of the patient as a whole, should lead in the study of the diseases of his specialty, which are fast becoming the major ones not conquered in the medical world.

In the meantime, my congratulations to Colonel Ash and Dr. Muriel Raum for bringing out this beautiful Atlas. The text, which was written by Colonel Ash, is rightly colored by the pathologist's viewpoint; that is, his concept of the relative importance of disease processes on the basis of the vast material in the Armed Forces Institute of Pathology. Only those who have compiled a book themselves can understand the amount of work that went into producing this text for the neophyte in pathology, as requested by the American Academy of Ophthalmology and Otolaryngology. Advanced students should realize that Colonel Ash's general remarks were not prepared for them. Let them study the plates, which were designed by Doctor Raum for students at all levels. This is as comprehensive and accurate a book as ever has been assembled on pathology for the otolaryngologist.

As Chairman of the subcommittee which was to guide the creation of this book, I regret only that we have not been of more help to the authors. We have done little more than criticize. Although a few solid contributions have been made by individuals, such as Dr. Stacy Guild, Dr. Paul Holinger, and especially Dr. Herman Semenov, there are but two people who have made this Atlas possible—Colonel Ash, with the extraordinarily able collaboration of Dr. Muriel Raum. The Committee has asked me to convey thanks to all concerned and is glad that the colossal task of collecting material for this comprehensive Atlas of Otolaryngic Pathology is finished for the present. We are looking forward to many printings and eventually a new edition, which is inevitable on a subject of such pressing and general interest.

EDMUND P. FOWLER, JR., M.D.
Chairman, Sub-committee on
Otolaryngic Pathology.

PREFACE

This Atlas of Otolaryngic Pathology is an effort to make available in convenient form as much of the pathology of the specialty as is practicable. This project had a humble beginning in 1937, when the American Academy of Ophthalmology and Otolaryngology sponsored the preparation, in what was then the Army Medical Museum, of study sets of slides with an accompanying syllabus for the use of candidates in preparation for the Board examinations. The syllabus passed through two editions of expanded publication in Atlas form. These were produced in the hectic war years when mechanical facilities were limited, and it was realized from the start that, while helpful, they were incomplete.

Toward the end of the war, a start was made at a more comprehensive coverage of the pathology of the regions involved. Material as it came to hand was set aside. Considerable impetus was given the project when Major Herman Semenov was assigned for several months to the Institute. Although his activity was interrupted by his return to civilian life, his interest in the project has never flagged. Sporadic efforts to complete the collection of material continued. Very helpful in 1947, were those of Captain Jacob W. Old. Following his separation from the Service, there was again a lull until Dr. Muriel Raum was granted a fellowship in Otolaryngic Pathology at the Armed Forces Institute of Pathology by the Academy. With her advent the project really gained headway. The scope of the coverage and the excellence of the illustrative material that have been achieved, after years of effort and delay, are in large part due to her intelligent application and meticulousness.

Two objectives have guided the authors in the preparation of the Atlas—one, to make available to the clinical specialist, in as convenient a form as possible, the pathology of every condition that specifically or remotely concerns him. And two, to offer the general pathologist, in greater detail than elsewhere, the pathology of this particular specialty. To accomplish these objectives we have thought it necessary, in furnishing a background for the clinician, to include subjects that will seem to the general pathologist to be covered rather superficially. This refers particularly to the first section on General Pathology. On the other hand, we have gone into much greater detail than is necessary for the clinician alone in the coverage of the specific entities. This is largely for the benefit of the general pathologist. We have intentionally stressed in seemingly unnecessary detail those entities that, through long experience with the Registry material, have impressed us as puzzling to the general pathologist. Some of the emphasis is due also to the enthusiasm, natural to authors, about items in which they are particularly interested. As examples of this are the adenoid-cystic tumors, by the junior author, and the schneiderian and nasopharyngeal tumors by the senior author.

Dr. Fowler, in his Introduction, has emphasized the importance of a background in pathology for the clinical specialist. That should be more impressive to the clinician than such a statement from an inevitably biased pathologist.

The Atlas format results actually in two books in one. The text, limited to a succinct background of general information on the entities, including references to some of the pertinent literature, is one book. It is not meant to provide the comprehensive coverage expected of a textbook or monograph. The second book is the collection of illustrations. While there has been an attempt to correlate text and illustrations, it has not been labored. It will be found, for example, that an occasional entity mentioned in the text is not represented by pictures because suitable material could not be obtained. On the other hand, the illustrations, by and large, cover the subject more comprehensively than does the text. To make them more informative, we have included clinical data in many of the captions. It is helpful to the clinician to understand the natural history of a disease or lesion, and certainly the pathologist should have all possible data on the behaviour and outcome of lesions with definite histologic characteristics. Incidentally, additional fine details in the illustrations can be seen through a reading glass.

It is obvious that this Atlas could be prepared only by the cooperation of a great many people. There are several persons, mentioned by Dr. Fowler, who have been of significant assistance, not only in furnishing illustrations but also in providing the clinical background, which we could not have. Particularly are we indebted to Doctor Herman Semenov for his help with the Section on Nose and Paranasal Sinuses; to Doctors Fowler, Guild, and Lindsay with the Section on the Ear, and to Doctor Holinger, with the Section on the Larynx. We have meant to give credit to contributors of individual cases that have been selected from the Registry material, and by references in the captions to credit publishers for illustrations that have appeared in journals or books bearing their imprint. No doubt we have committed omissions among the great number of illustrations, but none has been intentional. Most of the material has come from cases that were contributed routinely to the Registry of Otolaryngic Pathology; some has been obtained by specific request from individual pathologists and clinicians.

We are under deep obligation to those at the Armed Forces Institute of Pathology who were concerned with the mechanics of the project. Without Mrs. Helen Knight Steward's skilful editorial supervision there would have been many more faults. Mr. Lawrence Ambrogi and his assistants furnished us with excellently prepared slides from which to make illustrations. Without the facilities of the Photographic Department of the Institute under the direction of Mr. Roy M. Reeve, the Atlas would never have been possible. We are particularly grateful to Mr. Charles Edwards for his cooperation in taking photomicrographs and in preparing prints of the quality that is necessary for reproduction. Mr. Duncan Winter of the Medical Illustration Service has contributed his part in making complex illustrations more easily grasped by the reader. We can only acknowledge with gratitude the indulgence and patience of the Directors of the Armed Forces Institute of Pathology, Brigadier General Raymond O. Dart and Brigadier General Elbert DeCoursey, that have persisted through the long-drawn-out project. Doctor Benedict and the members of the Academy of Ophthalmology and Otolaryngology, who are directly concerned with the preparation of the Atlas, have also been indulgent. The authors hope that the results will prove worthy of the patience and tolerance of all those who have had part in the project, and that this Atlas will accomplish its objectives of bringing the otolaryngologist to a fuller realization of the importance of pathology as a background to his specialty, and the pathologist to a better understanding of the infinitely varied problems in this field of medicine.

J. E. ASH, COL. R.A. (Ret'd) M.D.

ARMED FORCES INSTITUTE OF PATHOLOGY
WASHINGTON, D. C.

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AN ATLAS
of
OTOLARYNGIC PATHOLOGY

CHAPTER 1

INFLAMMATION

Introduction —The pathologic processes involving specific anatomic areas cannot be appreciated without a background of general pathology. While it is not necessary to go into the minutiae, the basic principles applicable to the field of otolaryngology must be reviewed. One of the greatest difficulties experienced by one who has been away from the microscope for years is in recognizing the cells and other elements in tissue reactions. This section will present these details with the help of carefully chosen illustrations, and also the general aspects of specific diseases, tumors, dermatoses and tropical diseases unless they affect outstandingly a particular anatomic part. For instance, rhinoscleroma is placed in the section on nose, juvenile fibroma in that on the pharynx, and bronchogenic carcinoma in that on the lung. Such generalized conditions as tuberculosis, leukoplakia, leprosy and squamous cell carcinoma are treated in detail in this section, but reference is made to incidence and any special characteristics they exhibit in the ear, nose, and upper respiratory tract in the sections that deal with the pathology of these anatomic regions. This plan causes some duplication, but thereby general principles can be linked with specific entities. The histologic description of Boeck's sarcoid is included among the types of tubercles in this section, and the disease is discussed here, but additional illustrations will be found in the section on lymph nodes. In so far as possible, illustrations for this general division were chosen from instances of the conditions in the otorhinolaryngic field. This has augmented considerably the specific coverage. If one is interested in tumors that occur in the skin of the nose, he will find a series of unusual ones in the section on the dermatoses. Cross references are not generally included in the text, but the index will be a guide to the correlation of the material in the general and in the specific sections.

INFLAMMATION

Inflammation is conveniently divided into three phases, vascular, exudative, and resolution and repair. These stages are not sharply demarcated and the reaction is a continuous one, especially in bacterial injuries when there is sustained assault.

The main purpose of the reaction is to isolate and destroy the injurious agent. The intensity and character of the reaction, therefore, are modified by the kind and the degree of aggressiveness of the injurious agent and to some extent by the part of the body that is involved.

The primary reaction to injury, no matter what its cause, is vascular. It consists first in vasoconstriction, which is rarely evident clinically or pathologically, except in unusual injuries such as frost bite. There follows dilatation of the blood vessels which results in slowing of the flow of blood and this is responsible for the clinical redness and increased temperature of the part. With the slowing of the stream the leukocytes collect along the intima of the blood vessels, a phenomenon known as "margination."

The stage of exudation begins with the escape of various constituents of the blood through the walls of vessels. The character of the exudate depends on the type and severity of the injury. The simplest is the transudation of serum, producing EDEMA. When the serum is localized, particularly just beneath a surface, it is the clinical blister, bleb, or bulla. This is the chief reaction to certain injuries, such as a mild burn, thermal or chemical. Polypoid inflammations and polyps of the upper respiratory tract are pertinent examples of the effects of serous exudate into deeper stroma.

The next step is the migration of the **polymorphonuclear neutrophilic leukocytes** through the intercellular spaces of the vessel walls and their concentration at the site of injury. This is accomplished by their ameboid movement directed by the positive chemotactic influence of the damaged tissue. These cells are particularly prominent in bacterial injuries and are the type cell of acute inflammation. Their function is not only to phagocytize, but by their enzymes to destroy bacteria and to dissolve necrotic tissue. They are present in large numbers and themselves are undergoing necrosis from the bacterial or other toxic action. The result is pus, and the inflammation is called purulent. The pus cell is simply a neutrophilic polymorphonuclear leukocyte that is participating in the reaction.

Purulent inflammations are manifest clinically in a variety of entities:

1. FOLLICULITIS, when the inflammation is confined to a hair follicle. Acne is a more sustained lesion.
2. FURUNCLE, when the inflammation, primarily of the follicle, has involved the surrounding tissue but has been effectively confined to a limited area by a wall of exudate.
3. CARBUNCLE, essentially a group of furuncles welded into a mass by involvement of the intervening dermis.
4. CELLULITIS, a diffuse, purulent inflammation of the loose areolar tissues. It is particularly danger-

ous because it may travel for a great distance before meeting a natural barrier, as in the scalp and mediastinum.

5. ABSCESS, a localized collection of pus without particular relation to anatomic structure, e.g., peritonsillar, retropharyngeal.

6. PHLEGMON, a diffuse inflammation of solid tissues such as muscle and connective tissue. The involved elements are diffusely infiltrated with leukocytes and there is accompanying necrosis, but because of the nature of the tissue there is not the opportunity for abscess formation that there is in the looser areolar tissue and in some organs. Erysipelas is a specific example of a phlegmonous inflammation because it involves the skin as well as the subcutaneous loose tissues. Ludwig's angina is also, in part at least, a phlegmon.

Red blood cells escape by so-called diapedesis when the vessel wall is intact. When the vessel wall has been injured to the point of rupture the whole blood escapes. This is really not exudate but hemorrhage, especially when the vessel wall has been ruptured mechanically. There are certain types of infection that have a particularly destructive effect on the vessel walls, for example, plague, anthrax, and rickettsial diseases, and under these circumstances the resulting leakage of blood is called HEMORRHAGIC EXUDATE.

When the blood plasma escapes with its fibrin-forming ingredients, the exudate will contain fibrin fibrils in sufficient amounts to affect the consistency of the exudate. This is called DIPHTHERITIC INFLAMMATION. There are certain infections that are characterized by this type of exudate, diphtheria being the classic one. Infections caused by pneumococci and dysentery bacilli are other examples.

When a fibrinous exudate is developed in cavities, such as in the alveoli of the lung in lobar pneumonia, the involved portion becomes fleshy in consistency and microscopically the fibrin fibrils are seen in great abundance as a supporting meshwork for the other portions of the exudate. Fibrin fibrils can be distinguished from those of connective tissue and reticulin by the presence of little dots where the fibrils cross —nodal points—and by the presence of fibrin asters which are formed by the bunching of the fibrils about a central mass, probably a platelet. When the exudate is on a surface, as in pleurisy or diphtheria, the fibrin converts the exudate into a false membrane.

A few acute inflammatory reactions are characterized by **large mononuclear cells, histiocytes** or **macrophages,** rather than by exudate. Typhoid fever is the best example of such an acute inflammation. In bacillary dysentery the macrophage is a prominent feature.

The **interstitial endothelial cell or histiocyte** is a very important part of the body's defense mechanism. This is evident by its prominence not only in the acute infections but in chronic infections of various categories.

ORGANIZATION AND REPAIR

In every inflammation, even in the rare instances where there is no appreciable destruction of tissue by the injury and healing is by "first intention", there is proliferation of fibroblasts and vascular endothelium. These invade the exudate, hemorrhage, and damaged tissue to revitalize it and to repair the damage. This combination of young connective tissue and new blood vessels is GRANULATION TISSUE. The organization and attempt at repair progresses even with the persistence of the infection. The new tissue and the fresh exudate eventually are able to isolate the infection if the outcome is to be favorable. This combination of granulation tissue and exudate lining a cavity or surface is called PYOGENIC MEMBRANE and is found lining all abscess cavities and sinuses. At times, particularly on a surface, the granulation tissue develops in excess (proud flesh), interposing a hindrance to the healing, particularly to re-epithelization. The growth of the granulation tissue is at times so aggressive as to simulate malignant tumor. Examples of this are included among the following illustrations.

With the elimination of the infection or the injuring agent, granulation tissue has an opportunity to replace any lost tissue that is not replaceable by the proliferation of the specific tissues. Smooth and striped muscle, nerve fibrils, bone, cartilage and epithelium are capable of repairing defects in kind.

This replacement is not always in exact kind or amount, however. In the repair of a bone fracture there may be exuberant callus, and in the repair of injury to the periosteum, an over-production of osteoid tissue as in frontal osteomyelitis. In the repair of striped muscle there are bizarre multinucleated masses of muscle protoplasm, and in the re-epithelization of a surface defect the epithelium may be of the original or of another mature type, or of an undifferentiated type. For example, squamous epithelium may replace respiratory epithelium, a common phenomenon in the upper respiratory tract. This alteration from one type of tissue to another, under any circumstance, is termed METAPLASIA. Another example of metaplasia is the development of cartilage and bone in inflammatory connective tissue in situations where these elements are not normally present. This ability to change in type is a limited one and is possessed only by certain epithelia and connective tissues. Highly differentiated cells, such as nerve cells and striped muscle cells, cannot change their character.

Mucosal epithelium, more than other tissues, possesses the ability to change character. Change of the epithelium of the cervical and prostatic glands to squamous type, and change of the respiratory epithelium to squamous, transitional, or glandular types are common. The normal epithelium of these parts is still not too securely fixed in its specialization. It readily succumbs, therefore, to the influences of chronic inflammation, vitamin deficiencies, especially of A, of hormones, and of neoplastic incitors. The metaplasia of fibrous connective tissue to cartilage and bone is probably dependent on the close chemical relationship between the intercellular substances, collagen, chondromucin and osteomucin. A little disturbance in the chemical organizers can bring about significant alteration in the intercellular material.

A common development, particularly in chronic ulcerative processes as a result of the attempt at re-epithelization, is hyperplasia of squamous epithelium at the edges of the ulcers, with large pegs extending deeply into the tissues, at times showing mitotic figures and some immaturity in the cells. This is called PSEUDOEPITHELIOMATOUS, or better, PSEUDOCARCINOMATOUS HYPERPLASIA and, most disconcertingly to the pathologist, frequently simulates squamous cell carcinoma.

Granulation tissue is bound to result in more or less SCARRING. With the maturation of the connective-tissue element and the accumulation of collagen and reticulin, the vascular elements become less and less conspicuous. Harmful deformities result from the propensity of this aging connective tissue to contract. The large mononuclear cell or reticuloendothelial cell is an important factor in the formation of scar tissue. The reticulin fibers produced by these cells fuse to form thick fibers indistinguishable under ordinary conditions from collagen fibers of fibrous tissue. This is well illustrated in the thick basement membrane of allergic rhinitis. The relation between reticulin and collagen is not clear at this time.

CHRONIC INFLAMMATION

The type cells of chronic inflammation are the **lymphocyte** and **plasma cell.** They begin to make their appearance early in any inflammatory reaction and increase in number with time. In certain situations, particularly in the respiratory mucosa, these cells are the predominant elements in any inflammatory reaction, even an acute one, and they give to the tissues a characteristic appearance that can be identified even under the low power of the microscope. Purulent exudate has a granular appearance from the multilobed nuclei of the leukocytes and from the nuclear fragments. The chronic exudate, on the other hand, has a more uniform appearance because of the similarity in size, shape and chromatin content of the nuclei of the lymphocytes and plasma cells.

In any chronic inflammation in which plasma cells play an important role, peculiar structures called RUSSELL-FUCHS BODIES will be found. These are small, round or geometric, bright-red crystalline masses that are products of deteriorated plasma cells, developing probably from polysaccharides in their cytoplasm. They are particularly common in rhinoscleroma and were formerly considered of diagnostic importance. They are found, however, in any chronic inflammation in which the plasma cell is present in abundance. What is interpreted as an earlier stage of the Russell body is the PLASMACYTOID BODY. This is a cell somewhat larger than the normal plasma cell and filled with uniform, closely packed, eosinophilic globules. The sequence of development is presented in the color plate of cells.

Eosinophils.—The eosinophilic leukocyte may be the polymorphonuclear cell from the peripheral blood or a mononuclear cell, so-called tissue eosinophil. The function of these cells is not known although they will phagocytize to a limited extent. They are characteristic particularly of active allergic inflammations and of certain parasitic infections. It is assumed, therefore, that their function is concerned with reaction to allergens.

Basophils. — The basophilic polymorphonuclear cells of the circulating blood seem to play no part in inflammations, but the tissue basophil **(mast cell)** is a characteristic feature in certain chronic inflammations, most strikingly in urticaria pigmentosa. In this disease the dermis is densely infiltrated with mast cells which usually are round, about the size of a polymorphonuclear neutrophil, with a centrally placed, round or ovoid, vesicular nucleus. The cytoplasm by appropriate stains is found to be largely occupied by small irregular granules which take the basophilic stain. Their histogenesis is still in doubt. They do not come from the circulating blood and it is supposed that they are of connective tissue origin. They are rich in heparin. The basophilic blood cell plays a prominent part in granulocytic leukemia.

Plasma Cells.—The plasma cell is phagocytic although not actively so. In typhoid fever, for example, it is one of the first localizations of the bacillus. More important, these cells apparently are concerned with the development of antibodies. This may account for their prominence in inflammatory conditions of the upper respiratory tract.

Giant Cells.—When a foreign particle is too much for the leukocyte and the macrophage to handle, giant cells develop about it, chiefly by fusion of macrophages. These are called FOREIGN BODY GIANT CELLS and are similar in structure to those seen in the granulomatous infections where they are called the LANGHANS GIANT CELLS. They vary in size, and at times, as in tuberculosis, the cytoplasm may extend for some distance as pseudopods. The nuclei cells, but may be distributed around the peripheries. The Langhans type is regarded as a foreign body giant cell.

Another form is the multinucleated OSTEOCLAST whose specific function is to destroy mature bone. It is thought to develop from the osteoblast and is identified not only by its associations but also by the distribution of its nuclei, which is generally throughout the cytoplasm rather than peripheral as in the foreign body giant cell. This is the type cell of the giant cell tumors of bone, of tendon sheaths, and of the gingival epulis.

A third type is the malignant TUMOR GIANT CELL. This occurs in a variety of tumors, rhabdomyosarcoma, osteogenic sarcoma, and even in anaplastic carcinoma. It is characterized by great irregularity in size and shape and by a moderate number of nuclei of atypical size, shape, and chromatin content.

The TOUTON GIANT CELL is seen particularly in the xanthomas of the skin and tumors of tendon sheath. It is characterized by a peripheral circular arrangement of nuclei, a more or less foamy cytoplasm, and a serrated cell border.

The BASOPHILIC MACROPHAGE, which is smaller than the other giant cells, has a lymphoid origin. Its cytoplasm is basophilic and there are usually not more than two or three nuclei. It is seen in several specific inflammatory reactions, especially in infectious mononucleosis, rickettsial and viral diseases, and also in lymphatic tissue reacting to irradiation. The Dorothy Reed-Sternberg cell of Hodgkin's disease is of this type, if not of the same origin.

CHAPTER 2

GRANULOMATOUS INFLAMMATION

A granulomatous inflammation is one in which the reaction to disease or injury is proliferative rather than exudative. The prominent cell is the **histiocyte,** a large mononuclear cell known under a variety of synonyms — macrophage, clasmatocyte, epithelioid cell, large mononuclear cell, etc. It is an endothelial cell, predominantly reticuloendothelial, and also the endothelial cell of the adventitia of blood vessels. Others not concerned in granulomatous reactions remain fixed but are actively phagocytic. The Kupffer cell of the liver is the best example of these. The endothelial cell lining vessels is also phagocytic. Ordinarily the wandering cells occur in characteristic groups to form a histologic unit, the TUBERCLE. The classic form is that associated with infections by the tubercle bacillus. It is only in such infections that the process is called tuberculous. Infections other than tuberculosis in which tubercles are a part of the histologic picture are called tubercular or tuberculoid.

In addition to the presence of the large mononuclear or epithelioid cells there are frequently Langhans or foreign body giant cells already described and varying proportions of lymphocytes, plasma cells and fibroblasts. As the age of the tubercle increases its center usually undergoes necrosis in various forms, as mentioned in the section on necrosis.

Not all granulomatous infections produce the circumscribed tubercle, but the reaction is more diffuse and consists almost entirely of the endothelial cells without giant cells. Among the chronic infections that show this reaction are leprosy, histoplasmosis, rhinoscleroma and leishmaniasis. Among the diseases other than tuberculosis and tertiary syphilis showing the tubercle reaction are tularemia, lymphopathia venereum, and certain mycoses, particularly blastomycosis and coccidioidomycosis. Foreign bodies will also stimulate granulomatous reaction. These include such exogenous matter as sutures, paraffin and other fatty and hydrocarbon substances, and endogenous material such as necrotic collagen, cholesterol crystals, and broken down fat. In these instances the giant cells form about particles too large for the single macrophage to handle. Certain foreign substances stimulate an aggressive, neoplasia-like reaction. The tubercles extend into contiguous tissue beyond the site of original localization. This is particularly true of vegetable and animal fats (lipoid pneumonia), paraffin (paraffinoma), beryllium from fluorescent lamps, and silica.

If the reaction is able to overcome the cause, the tubercle tends to become fibrotic and the necrotic material within may calcify, particularly in tuberculosis.

It is not possible always to determine the cause of a granulomatous reaction unless the etiologic agent can be demonstrated by culture, animal inoculation, or by direct microscopic examination. The tubercles of different etiologies can simulate each other exactly. For example, the granulomas of tularemia, lymphopathia venereum, and filariasis may be identical. They are characterized by a central stellate zone of necrosis containing abundant nuclear fragments, a surrounding zone of endothelial cells, and an outer border of lymphocytes and plasma cells. Giant cells are rare.

The endothelial cell participating in diffuse granulomatous reactions receives a special name in several diseases. Examples are the foamy Mikulicz cell in rhinoscleroma, the less foamy cell in leprosy (lepra or Hansen cell), and the typhoid cell in that disease.

The endothelial cell also participates in a number of systemic diseases that result from metabolic disorders. Among these are disturbed fat metabolism, the lipid reticuloendothelioses, Gaucher's disease, Neimann-Pick disease and Hand-Schüller-Christian disease, discussed in the section on lipoid dystrophies.

SPECIFIC GRANULOMATOUS INFLAMMATIONS

Tuberculosis. — Tubercle formation, ulceration and, less commonly, nonspecific exudate are evidences of tuberculosis of the structures in the field of the otolaryngologist. Since the disease involves chiefly the mucosae, except in the tonsils, the lesions are practically always ulcerative and may not be recognized as tuberculous. It should be suspected if the patient is suffering from active pulmonary disease, and the diagnosis is established by the identification of tubercle bacilli in smears or in a biopsy specimen. The diagnosis should not be made otherwise, because what might appear clinically to be a tuberculous lesion might well be some other disease, particularly syphilis or an early carcinoma. The tubercle in the larynx in the absence of active pulmonary disease would in all probability not be tuberculous, because in that situation the infection is practically always secondary to pulmonary tuberculosis. In the tonsil, however, the primary infection does occur in children, especially in foreign countries, and is usually of the bovine type.

Tuberculosis of the nose is rare even in active pulmonary infection, although primary infections have been reported. It is usually in the form of a smooth tumor on the septum. Such a tumor-like lesion is called a TUBERCULOMA. It is seen in forms ranging from superficial ulceration with metaplasia of the epithelium to the squamous type that becomes wart-like from hyperplasia. Infection may extend into the septum, particularly the cartilaginous portion, and produce perforation. When the tuberculoma is situated near the nostril the skin can be involved.

Tuberculosis of the paranasal sinuses is also rare, but when it does occur it may cause extensive destruction of the bone. This is particularly true when the ethmoids are affected, for the infectious process can erode into the orbit and cranial cavities. Tuberculous osteomyelitis of the maxilla may extend into the orbit. When the infection has reached the bones through the blood stream, osteomyelitis is the direct result. When, however, it extends to the cavities through the ostia via the mucosa, the bone is involved secondarily from a primary ulcerative process.

Tuberculosis of the oropharynx and fauces is less rare and in most instances is secondary to pulmonary disease. Clinically it is a superficial, progressive ulcerative process and tubercle bacilli can usually be found on direct smear. The ulcerated surface may become secondarily infected with Vincent's organisms, and their presence in smears may prove a diversion from the real nature of the lesions.

Szanto and Hollender (for reference see section on pharynx) reviewed a large amount of autopsy material and determined that the nasopharynx was involved in 75 per cent of tuberculosis of the oral and nasal regions. They emphasized the importance of recognizing the lesions, for they constitute a source of reinfection when treatment has been restricted to the pulmonary disease, and they provide a source of tubercle bacilli in the sputum when organisms are not being contributed by the lung lesions. The lesions are predominantly on the posterior part of the roof and upper part of the posterior wall, occasionally involving the ostia of the auditory tubes and the nasopharyngeal surface of the uvula and soft palate. These are all sites where the sputum, during coughing, is most forcibly projected against the mucosa. Clinically the lesions are either irregular ulcers with undermined margins and yellowish gray bases or are subepithelial collections of tubercles without ulceration.

The mastoid is occasionally infected either by blood-stream dissemination or from the middle ear. Fistulous tracts may develop through the bony capsule of the mastoid and labyrinth and empty onto the skin surface. In other instances where immunity is relatively high and there is chance infection of the middle ear or temporal bone, tubercles develop, but, in addition, hyperplasia of the bone and connective tissue elements may lead to eburnation of the bone and scarring that effectively limit the extension of the infection. Under these circumstances the seriously destructive involvement of the labyrinth that is otherwise possible, is rare.

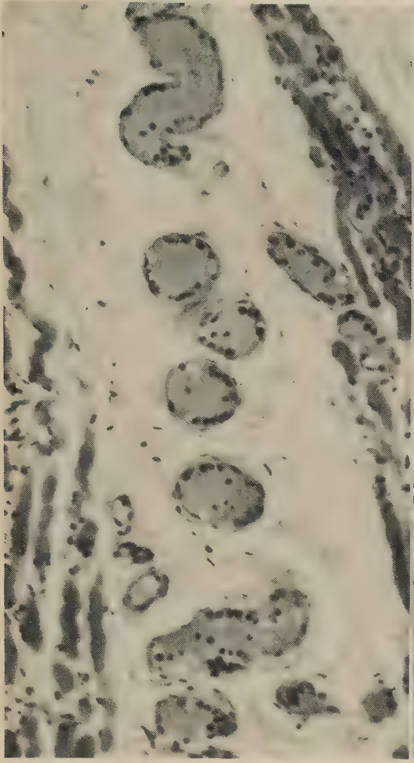
Tuberculosis is capable of inducing not only the granulomatous type of reaction but also an exudative one, particularly in the lining membranes such as the pleura. This exudative reaction may be induced in the mucosa of the ear, with destruction of the soft parts but little or no tubercle formation. It is only by the demonstration of the tubercle bacillus that the nature of the process is revealed.

Syphilis.—The PRIMARY LESION not uncommonly develops on the lip or tongue, less commonly on the tonsil, very rarely in the nose and then at the mucocutaneous junction. It is said that about 75 per cent of extragenital chancres are on the lips. The clinical features are the same no matter where it is located. There is a circumscribed, raised, characteristically indurated nodule with an ulcerated center. On the lip it may be mistaken for carcinoma because of its crusted, indurated character and refractoriness to local treatment. The clinical appearance of a chancre on the moister mucosa of the tongue and mouth may be altered by bacterial infection, but the induration will not be entirely disguised.

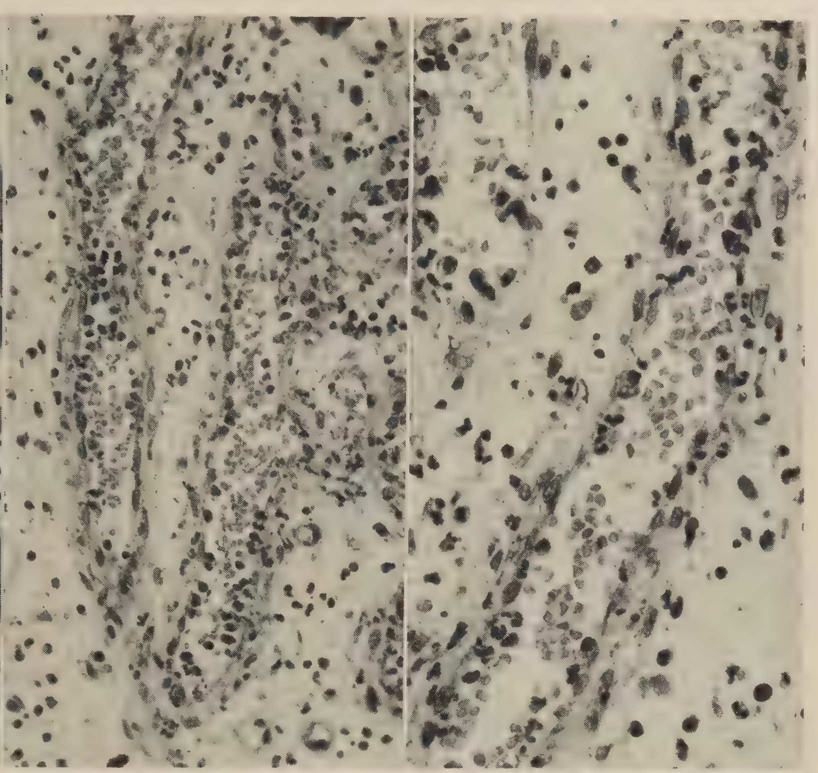
The induration is the result of the characteristically dense infiltration of the tissues by lymphocytes and particularly plasma cells. The suspicion of chancre can be obtained under the low power of the microscope from the density of the exudate. On closer examination it will be seen that the smaller blood vessels are involved. Exudate of the same type invades the walls and separates the components into layers. Accompanying this there is proliferation of the endothelium. The combination of these processes leads to occlusion of the vessels. *Treponema pallidum* can be demonstrated clinically by the dark field method and in the tissues by specific silver impregnation methods.

The epithelium associated with an ulcerated chancre of some standing usually shows hyperplasia, to such an extent at times that carcinoma may be suspected.

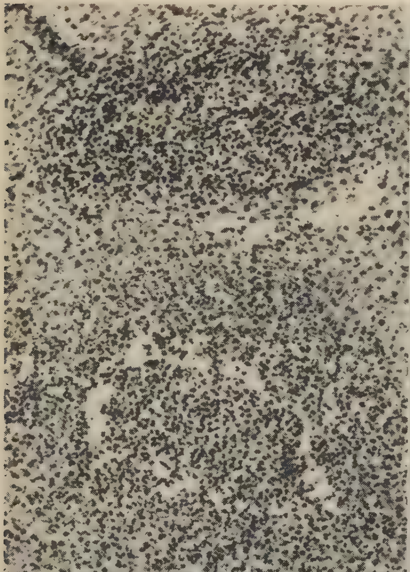
SECONDARY LESIONS are characterized by exudate predominantly of lymphocytes and plasma cells, not usually as dense, however, as in the chancre. Endothelial cells and an occasional giant cell may be included, and a certain amount of fibroblastic proliferation. The clinical differences in the skin lesions are dependent on the stage of development and the amount of exudate, but in all of them the plasma cell is a conspicuous element. As in chancre, the dense hyperplasia of the overlying epithelium may



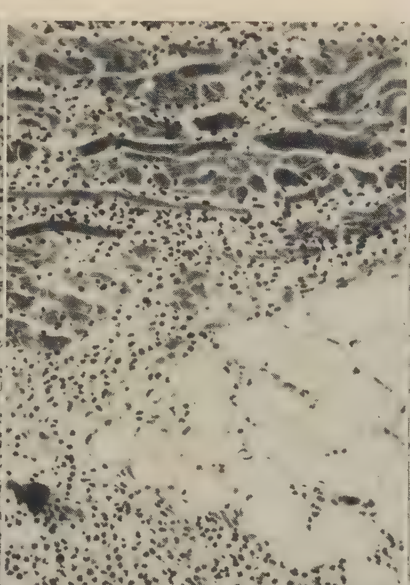
Vascular dilatation; margination of leukocytes along the intima. x 125.



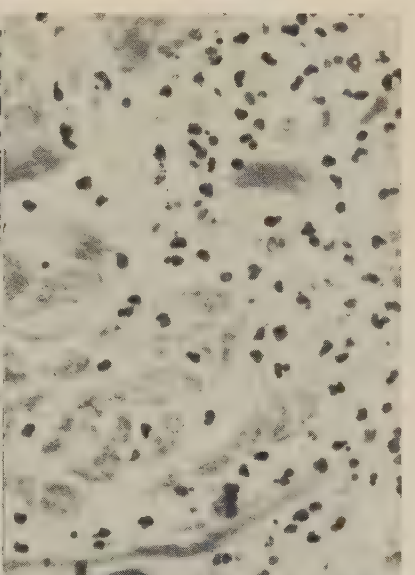
Migration of leukocytes. Leukocytes passing through vessel walls and others free in edematous tissue spaces. x 275 and x 400.



Abscess, tonsil. Massing of polymorphonuclear leukocytes and necrosis of tissue in center. Edge of follicle at top. x 125.



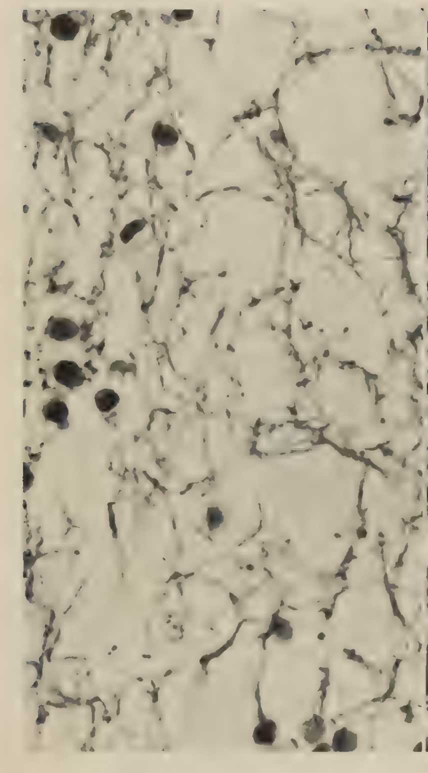
Cellulitis. Erysipelas. Leukocytes diffusely infiltrating edematous subcutaneous tissue. x 125.



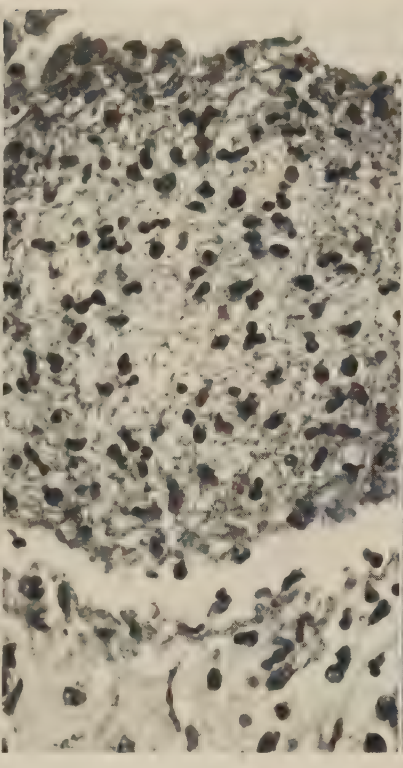
Phlegmon. Leukocytes infiltrating dense collagenous tissue. x 395.

INFLAMMATION

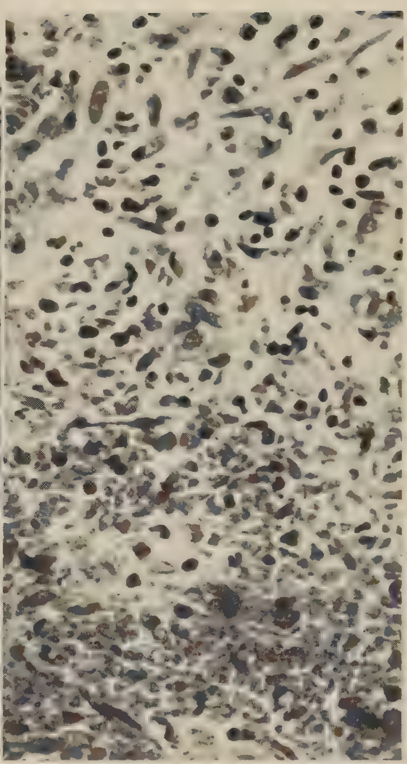
EXUDATES, ORGANIZATION



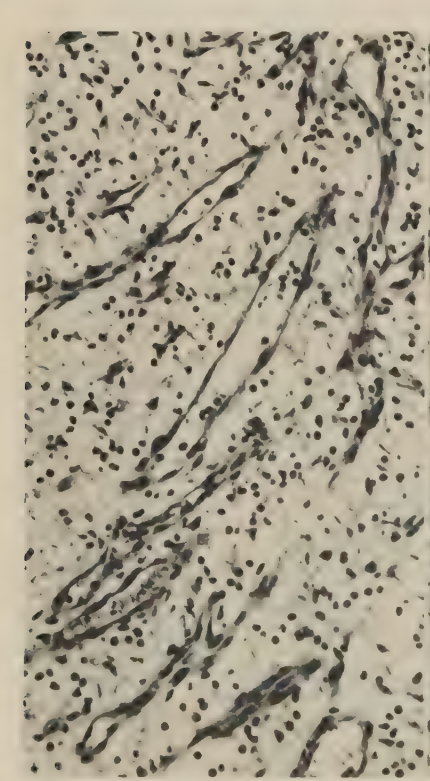
Fibrinous exudate showing nodal points and asters. x 605.



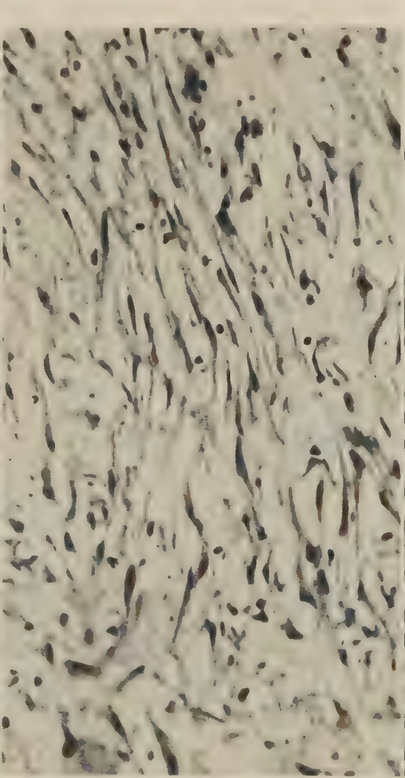
Diphtheritic exudate. Pseudomembrane above. x 400.



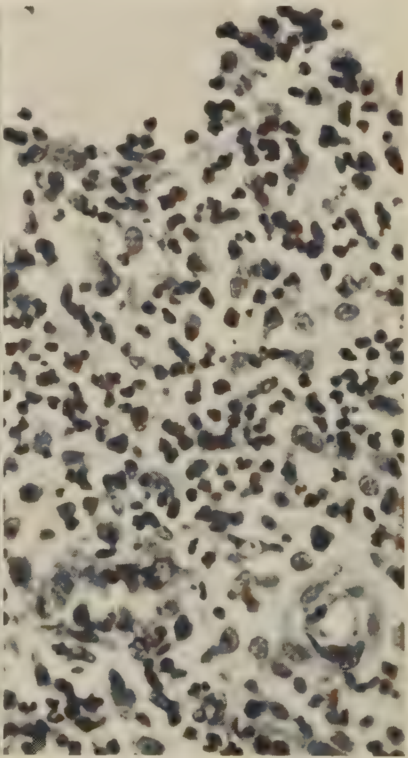
Hemorrhagic exudate. Blood below, organization above. x 400.



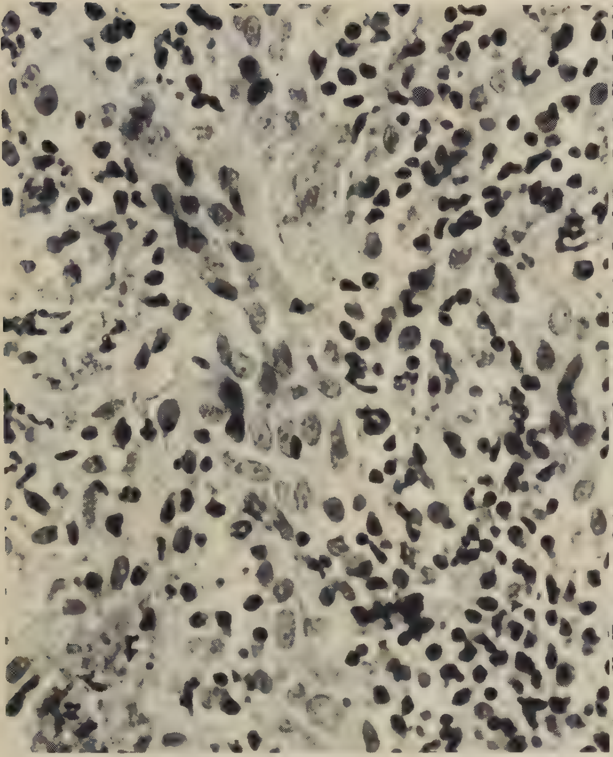
Organization. New blood vessels show endothelial buds. x 145.



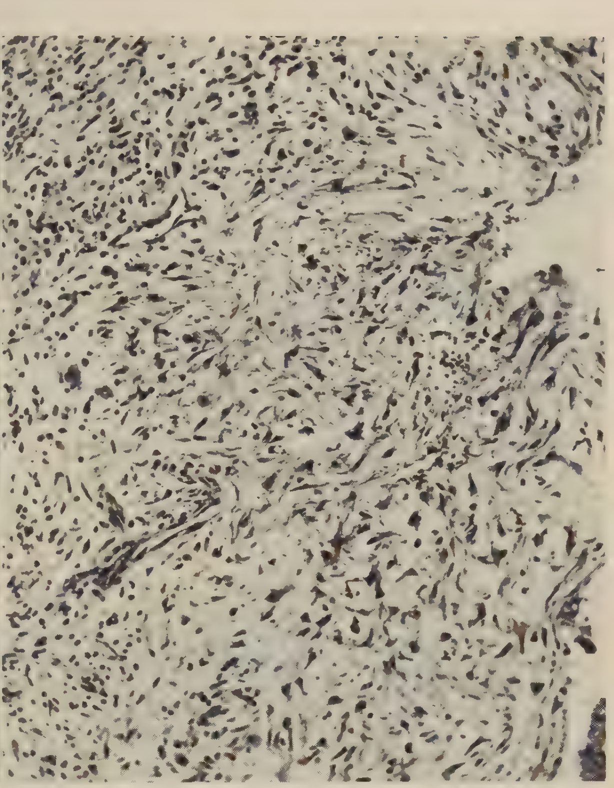
Young fibroblasts in granulation tissue. x 275.



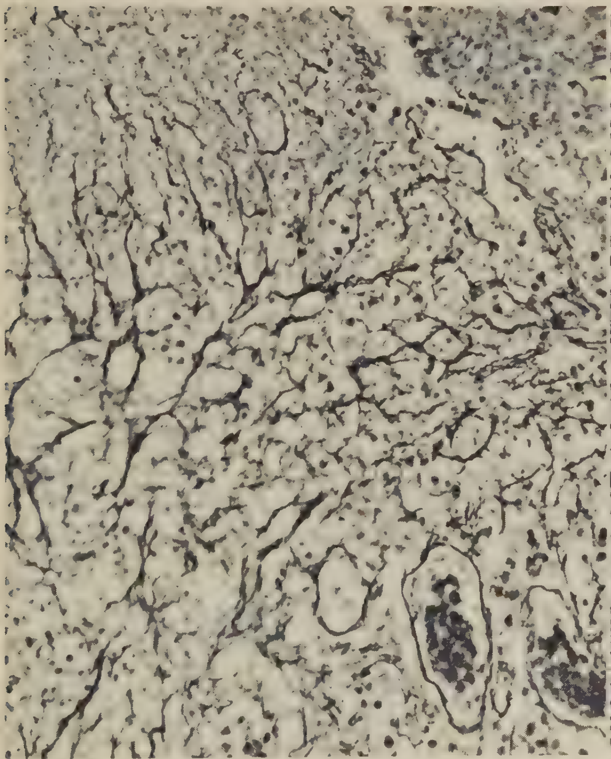
Pyogenic membrane. Granulation tissue infiltrated by leukocytes. x 400.



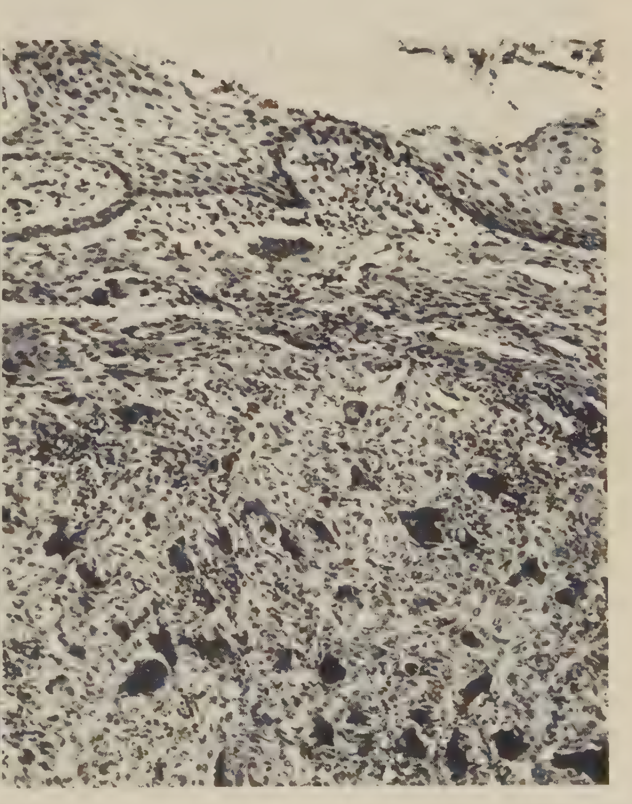
Vascular endothelium that may be mistaken for epithelium. x 395.



Dense granulation tissue from ear, resembling fibrous tumor. x 160.

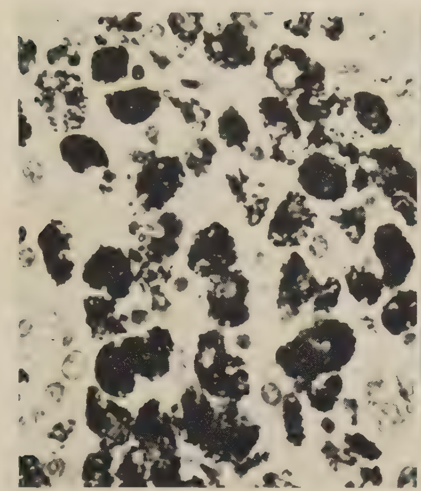


Distribution of reticulum in granulation tissue demonstrated by silver impregnation. x 220.

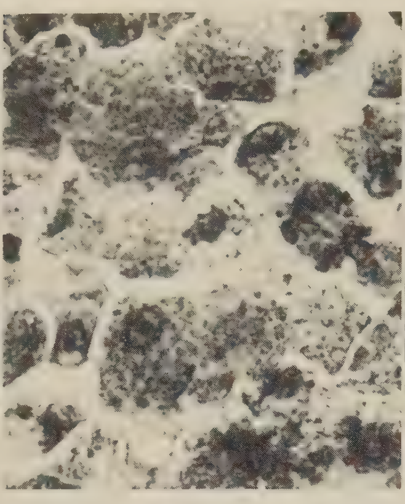


Fibrous-tissue and **giant-cell reaction** following tooth extraction. Gingival epithelium above. x 125.

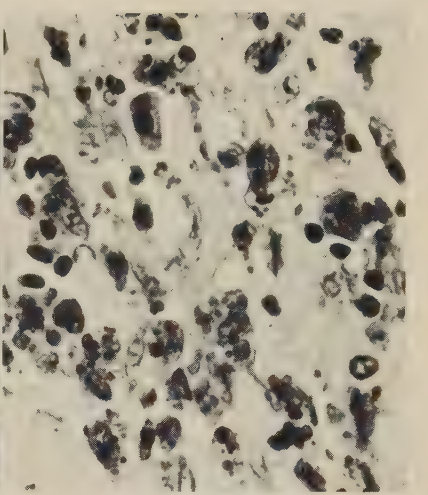
MACROPHAGES, ENDOTHELIAL CELLS



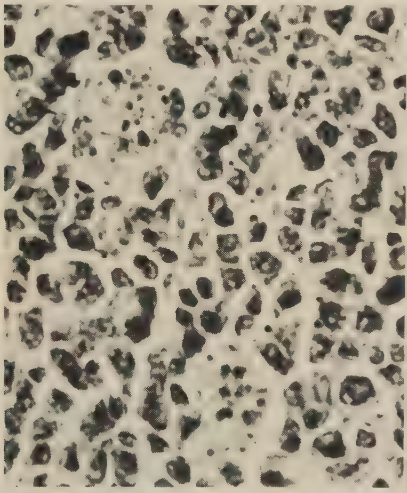
Macrophages:
Lung. Anthracosis, coal pigment. x 550.



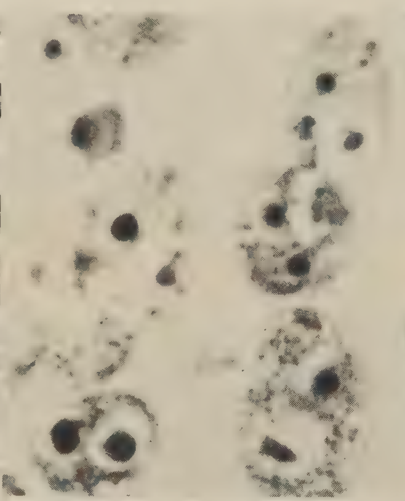
Lung. Dust cells in alveoli. x 900.



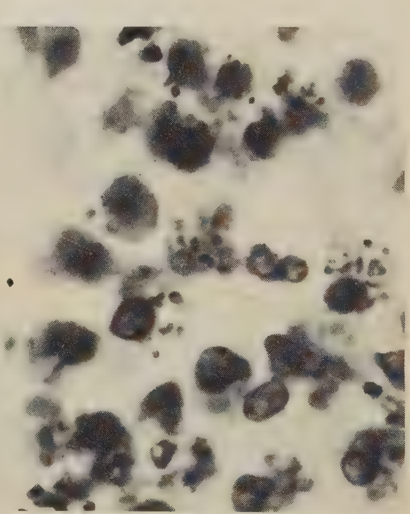
Old hemorrhage, hemosiderin. x 500.



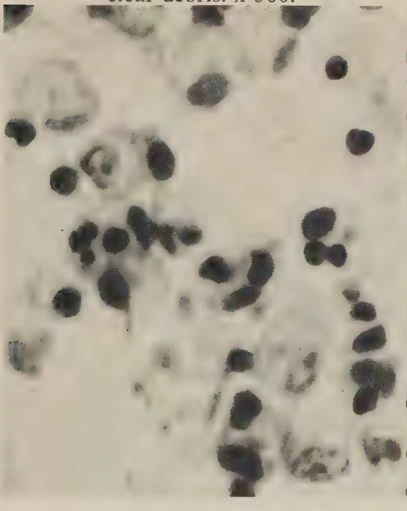
Macrophages:
Germinal center of lymph node. Nuclear debris. x 500.



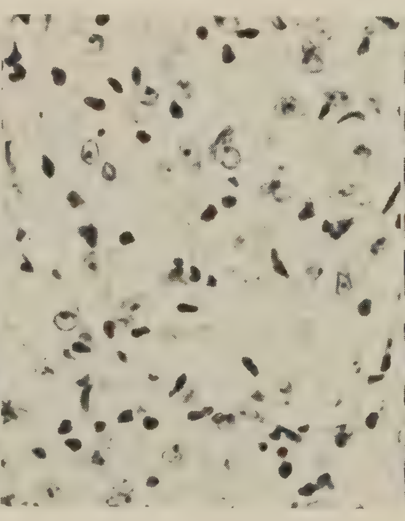
Stool, bacillary dysentery. Red blood cells. x 1,000.



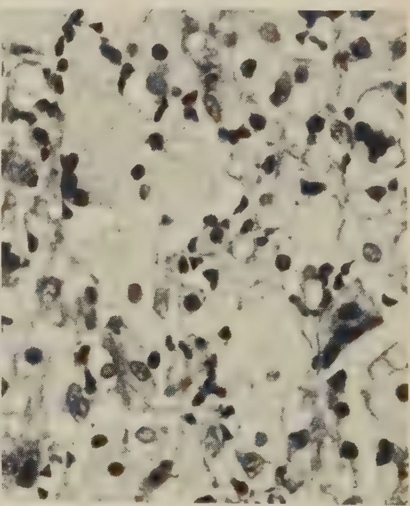
Infection. Bacteria. x 1,260.



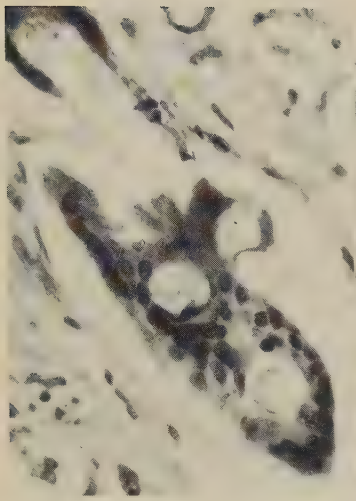
Endothelial cells:
Typhoid cell, in typhoid fever. x 1,000



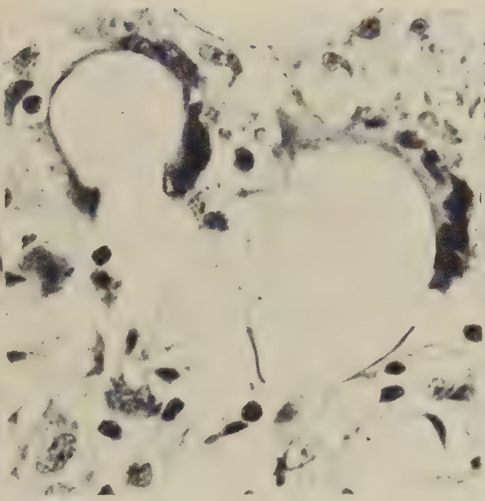
Epithelioid cell, in a tubercle.



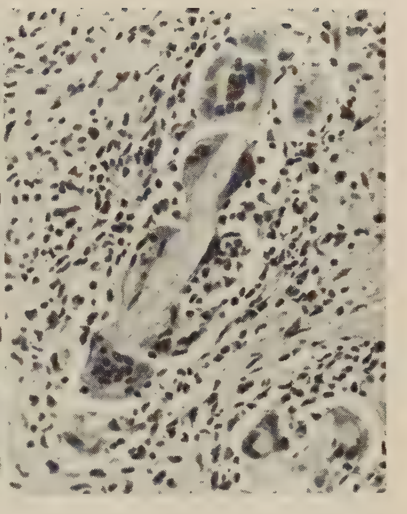
Xanthoma cell containing lipid, in tendon-sheath tumor. x 355.



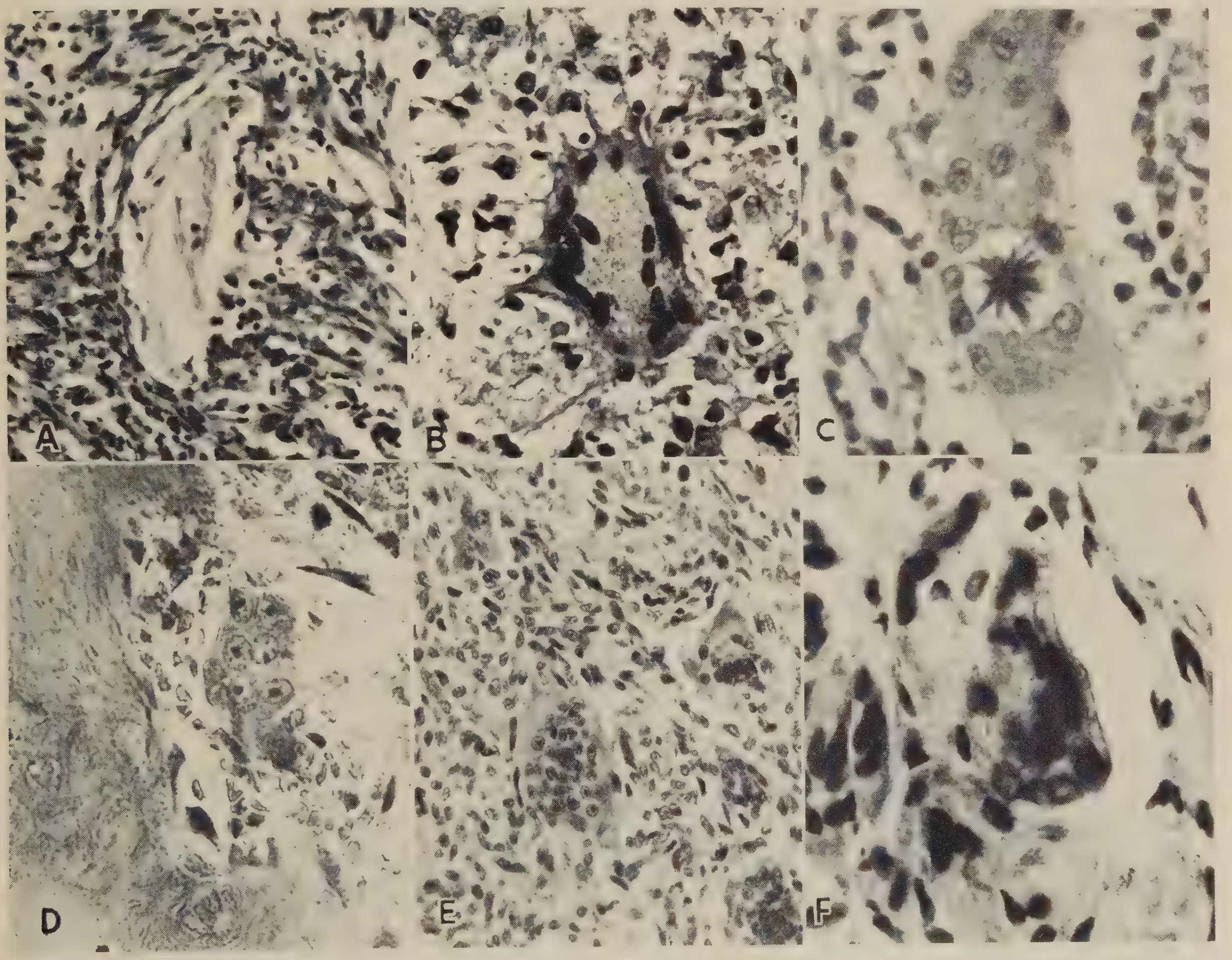
Cotton fiber within foreign body giant cell, brain. x 360.



Foreign body giant cells about globule in paraffinoma, nose. x 600.



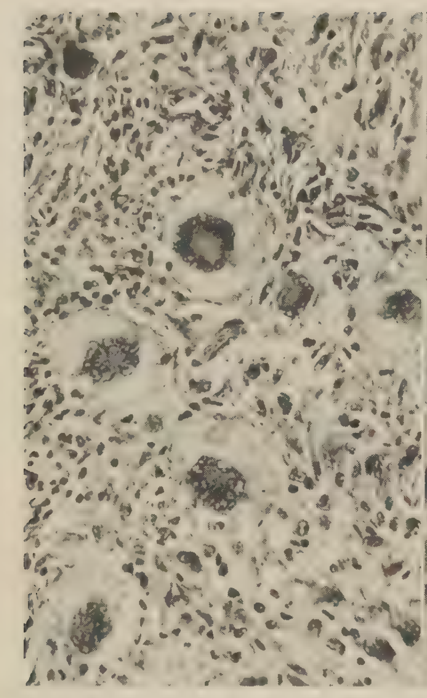
Several foreign body giant cells surrounding bone spicule, ethmoid sinus. x 200.



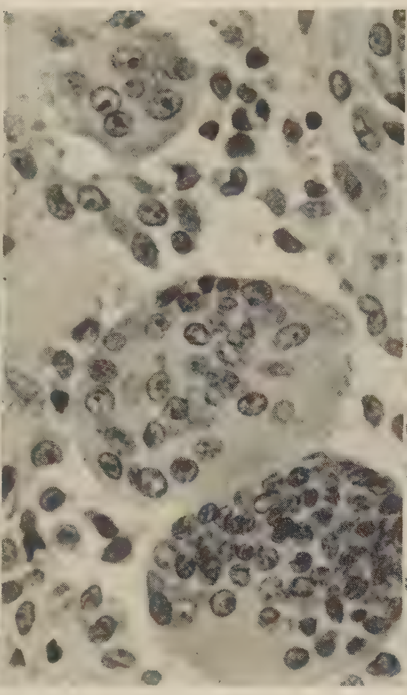
A. Foreign body reaction and giant cells about strands of keratin in middle ear. x 205. **B.** Langhans giant cell with prominent protoplasmic processes, in tubercle. x 475. **C.** Giant cell with asteroid in case of sarcoidosis. x 900. **D.** Osteoclast in bone lacuna. x 500. **E.** Cells in giant cell tumor of bone. x 275. **F.** Giant cell projecting into lumen of endothelial-lined space, epulis. x 650.

INFLAMMATION

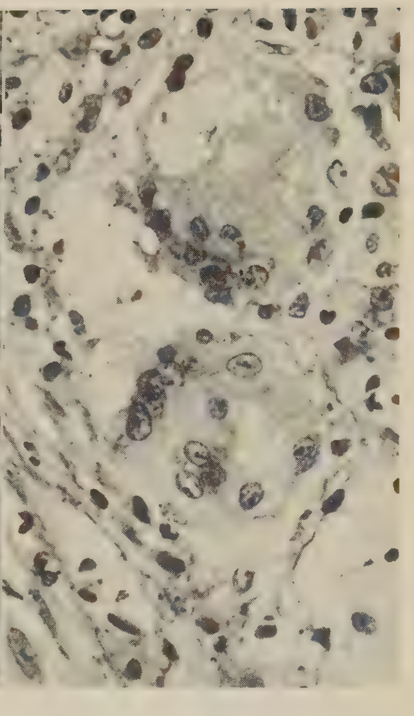
GIANT CELLS



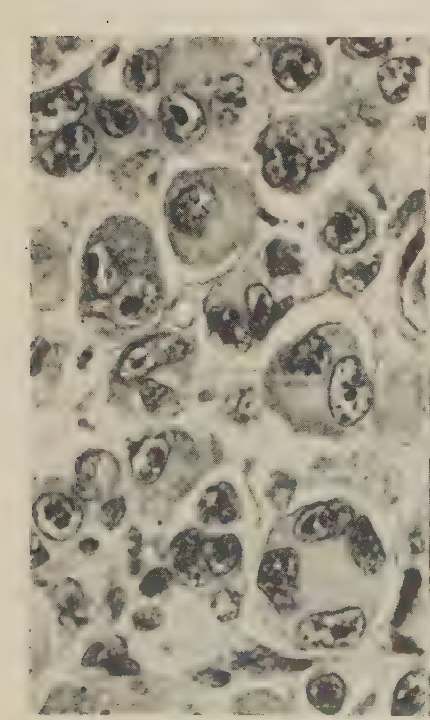
Touton giant cell, xanthoma, nose. x 220.



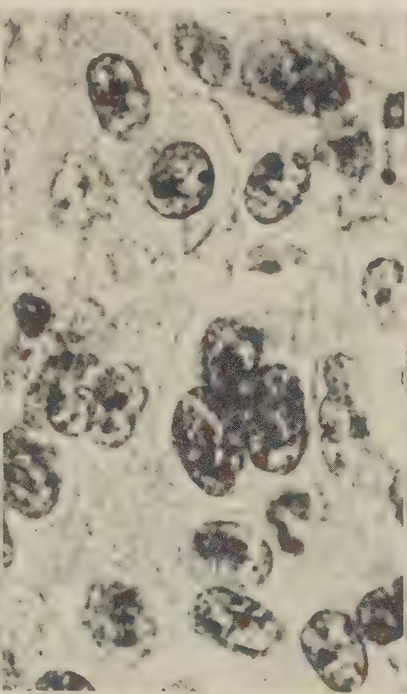
Tumor giant cells:
Tendon sheath, benign. x 500.



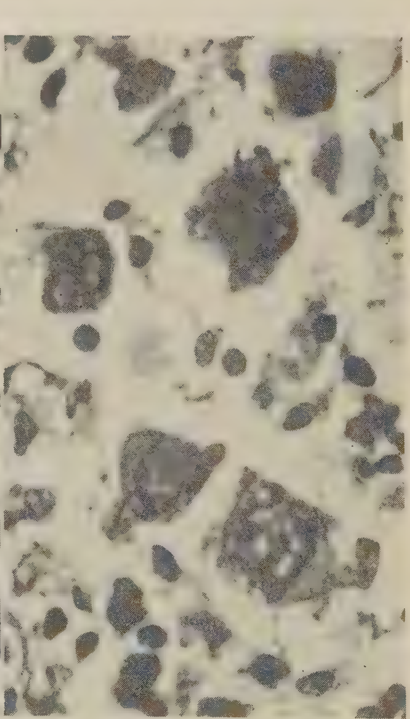
Tendon sheath. Irregular masses of lipid. x 400.



Tumor giant cells:
Malignant melanoma, nose. x 500.



Bronchogenic carcinoma. x 1000.



Reed-Sternberg, Hodgkin's disease. x 800.

advance to such an extent that the lesion may resemble the frambesia form of yaws.

The MUCOUS PATCH is an irregular area of superficial ulceration surrounded by an erythematous zone; the surface may be covered by dirty gray exudate. Mucous patches on the oral and pharyngeal mucosa are about as common as the secondary skin manifestations. Histologically, the exudate is similar in content to that of the chancre, but there is not the dense packing of the cells. The obliterating vasculitis seen in the chancre is found also in the secondary lesion. Syphilis is predominantly a disease of the blood vessels.

Another type of skin and mucous-membrane reaction is the CONDYLOMA LATUM. This is a papillary structure formed by elongation of the papillae of the skin and corresponding lengthening of the rete pegs. The dermis is edematous and infiltrated with inflammatory cells, including polymorphonuclear leukocytes, but with the usual predominance of the plasma cell. Condylomas may form on the epiglottis or on the laryngeal mucosa and in the external auditory canal.

TERTIARY LESIONS, which may not appear for years after the earlier evidence of infection, represent the granulomatous stage of the disease. Those involving deeper tissues can be very destructive. There is a tendency to spontaneous regression of the gumma, but it results in scarring and deformities.

The gumma is a comparatively rare manifestation of syphilis in present times. More common is a diffuse or focal, chronic, less specific, interstitial inflammation, particularly in such common sites of localization as the aorta and leptomeninges. The plasma cell and lymphocyte, as well as the proliferative endarteritis and endophlebitis that are seen in the chancre, are features of this tertiary lesion.

The GUMMA, while following generally the pattern of the tubercle of tuberculosis, has several distinctive characteristics. The central necrosis is firmer, more gelatinous than caseous, and the whole lesion has a rubbery consistency, hence its designation. The gumma enlarges by an extension of the process rather than by fusion of independent tubercles as in tuberculosis; giant cells as a rule are less conspicuous, and the epithelioid-cell zone is vascularized. The tuberculous lesion is avascular.

The advent of effective treatment of syphilis has made reinfections possible.

Congenital Syphilis.—There has been a great decrease in the incidence and in the severity of congenital syphilitic lesions since the introduction of modern treatment and with the better supervision of the prenatal period. The four general types of lesions are: 1, acute inflammatory reaction, including polymorphonuclear leukocytes; 2, subacute or chronic interstitial inflammation, with lymphocytes and plasma cells predominating; 3, gumma; 4, congenital defects secondary to the inflammatory lesions. Lesions of the fourth type are typically exemplified in the Hutchinson's teeth. There is hypoplasia of the deciduous second molars and of the permanent incisors and first molar teeth. The incisors are characteristically notched, with the notch representing a large segment of a small circle, differing in this way from the rachitic notch which is a small segment of a large circle. The molars are nodular—"mulberry molars." The teeth generally are short and have relatively narrow occlusal surfaces — "pegged teeth." Aside from the more marked and typical effects on the long bones, such as saber shins, there may be focal or diffuse resorption of the flat bones of the skull.

A localization of interest to the otolaryngologist is the ear in which nerve deafness occurs in a small percentage of cases. The cochlea is involved in miliary gummatous inflammation and in subsequent fibrosis. There is stenosis and ectasia of the cochlear duct with atrophy of the specialized epithelium. The bony canals become narrowed as a result of periostitis. The spiral ganglia and the ganglia of the 8th nerve are involved in an inflammatory reaction consisting of lymphocytes and plasma cells. In addition, there may be gummatous osteomyelitis in other portions of the temporal bone.

The more active lesions are those of the mouth and pharynx that are comparable to the mucous patches of acquired syphilis. The mucocutaneous junctions are involved, resulting in scars about the corners of the mouth and the nares (rhagades).

Histologically, the lesions of the skin show an infiltration of lymphocytes and plasma cells sufficiently active to cause rupture of the skin, producing fistulae. These are replaced by collagenous scar tissue.

DUBOIS' ABSCESS of the thymus is regarded as a characteristic lesion, but it is rare. It develops in the central part of the gland from necrosis of the epithelial nodules of the thymus, and the necrotic areas coalesce to form a gross lesion. The cavity is lined by reticulum cells and contains thick, yellow, nonpurulent fluid. Accompanying the necrosis is a fibrous repair of the defect.

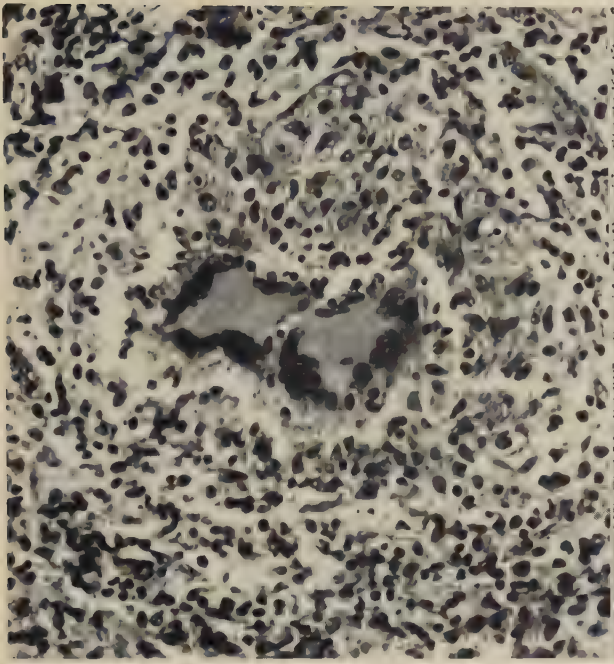
Sarcoidosis (Boeck's sarcoid), a granulomatous reaction of controversial etiology, is still regarded by some as a hyperergic reaction to a tuberculous infection. Originally the condition was described as separate entities as it affected different parts of the body. Uveoparotitis, sarcoid of the skin, the bone lesions manifested particularly in the digits, and the lung involvement were described as separate diseases. It is accepted now that these are all manifestations of the same condition. Any part of the body can be involved, including the ear and nose, and sarcoidosis must be considered in the differential diagnosis of a granulomatous inflammation of any region. It is not possible, however, to make the diagnosis on histologic grounds alone. The whole clinical and pathologic picture must be appraised and specific etiologic possibilities excluded.

The disease is characterized histologically by tubercles composed of reticulum cells (epithelioid cells) and a few giant cells, but with practically complete absence of necrosis. The tubercles are usually much smaller and more sharply defined than in tuberculosis. Reticulin fibers, which are not present in tuberculosis, can be demonstrated among the cells of the tubercles. Tubercle bacilli are not demonstrable either by direct examination or by animal inoculation. The so-called SCHAUMANN BODY, once regarded as a diagnostic feature of sarcoid, can be found in other granulomas. This is a stellate, cockleburr, or crystalline particle, presumably developing from lipid-proteins of deteriorating cells.

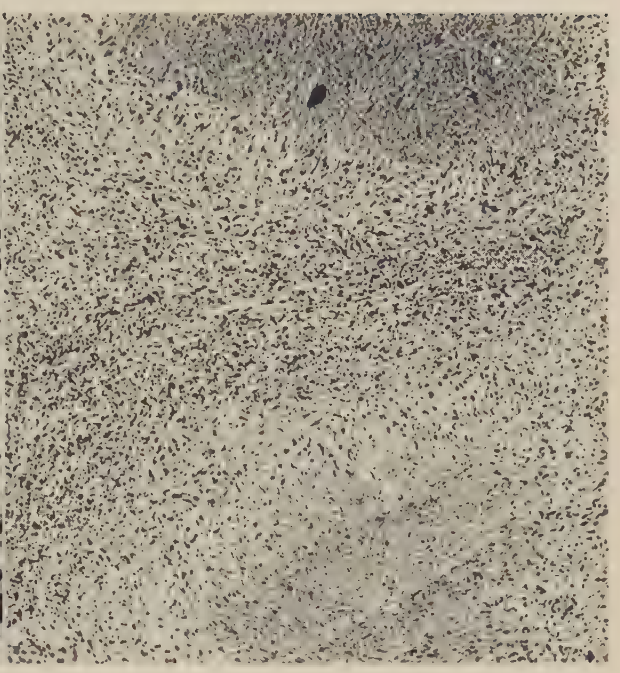
The disease runs a chronic course and may terminate spontaneously. Active tuberculosis is occasionally a complication, particularly of the sarcoid dermatosis in young colored females.

Boeck's sarcoid is not a particular problem of the otolaryngologist except when the skin of the face, the tonsils, and the cervical lymph nodes are affected. The nasal septum and other parts of the nose, as well as the salivary glands, are sometimes involved. Such a syndrome is analagous to that of Mikulicz' disease.

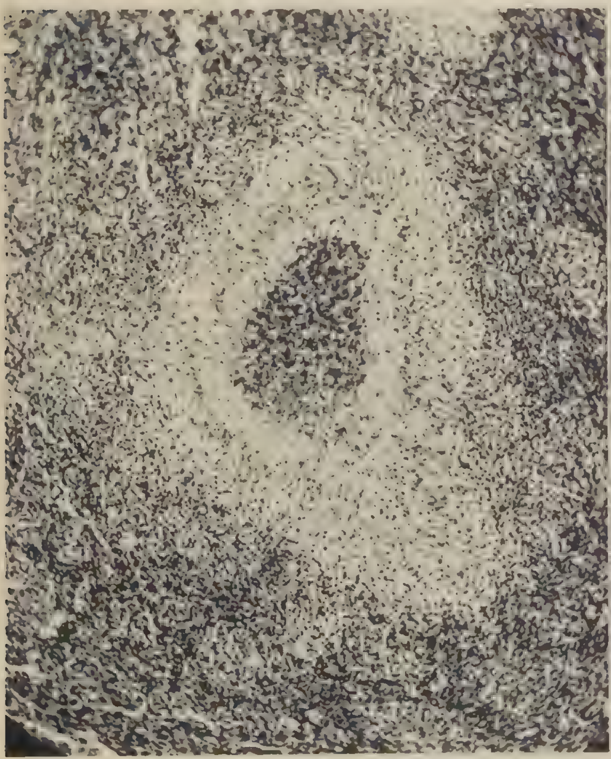
TUBERCLES–INFECTIOUS GRANULOMAS



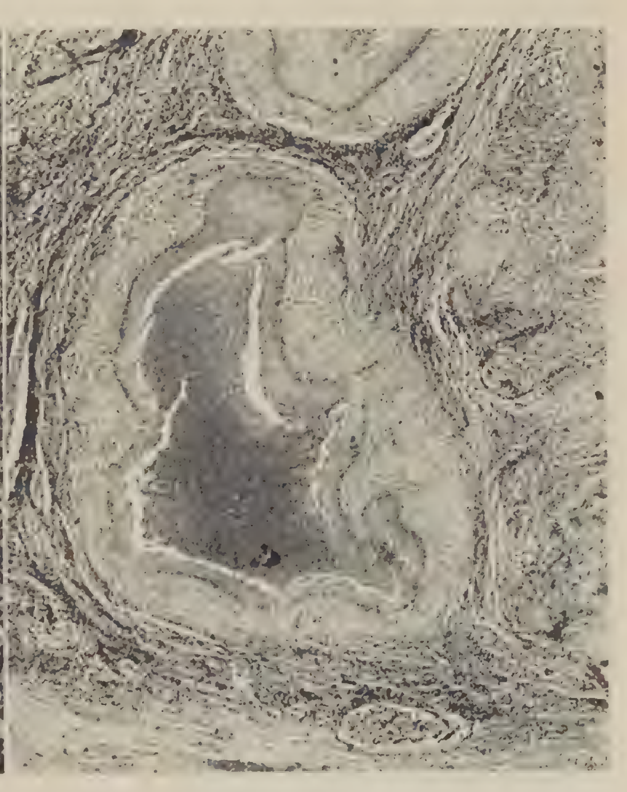
Tuberculous mastoiditis. Langhans giant cells in center; surrounding mass of epithelioid cells; outer layer of lymphocytes and fibroblasts. x 400.



Syphilitic gumma, heart. Central area of necrosis with outer zone of proliferating fibroblasts and capillary vessels, some extending into necrotic area. x 70.

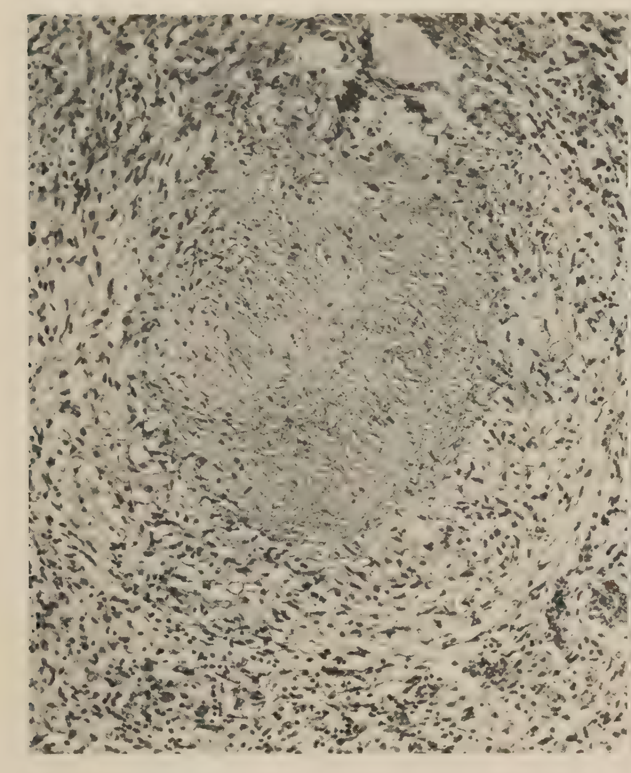


Tularemia, lymph node. Necrotic leukocytes surrounded by radially arranged epithelioid cells. x 120.

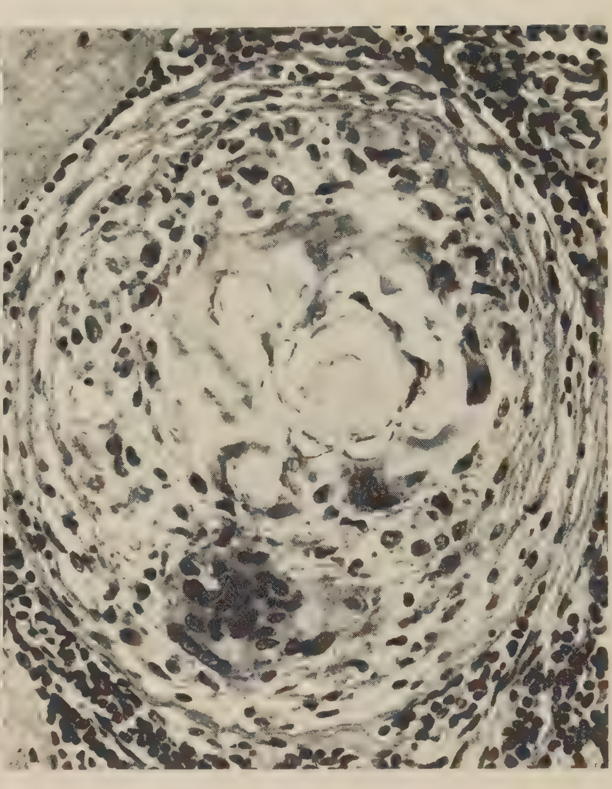


Lymphopathia venereum. Stellate abscess with purulent center, surrounded by zone of palisaded epithelioid cells and outer zone of lymphocytes and plasma cells. x 28.

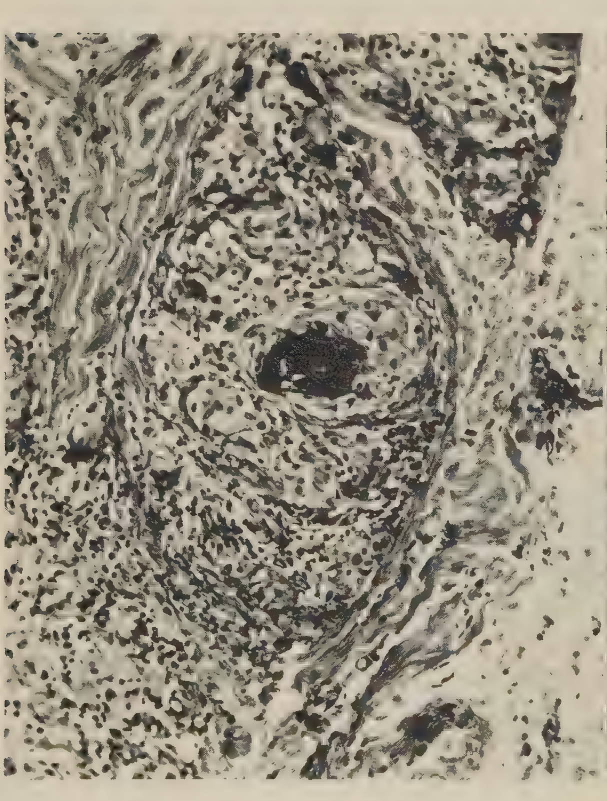
INFECTIOUS AND FOREIGN BODY GRANULOMAS



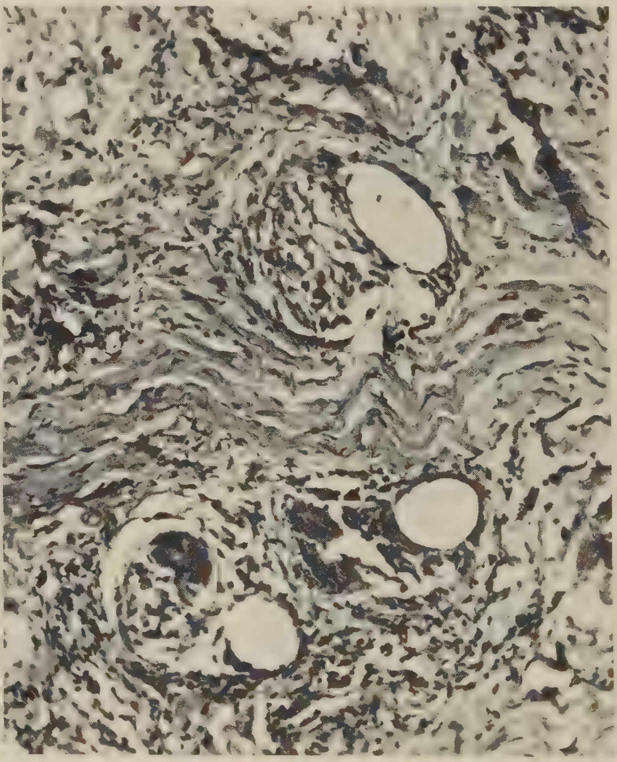
Tuberculosis. Fibrosing tubercle. Fibrous capsule forming about central area of caseation necrosis. x 125.



Sarcoidosis. Circumscribed lesion composed of epithelioid cells and giant cells. Schaumann body in center. No caseation necrosis. Early fibrosis. x 400.

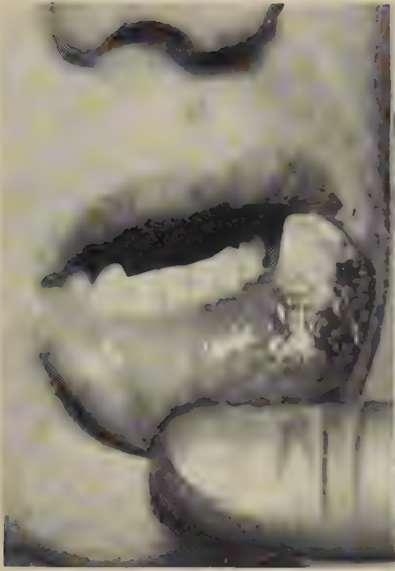


Foreign body granuloma around particle of dirt in subcutaneous tissue. x 100.

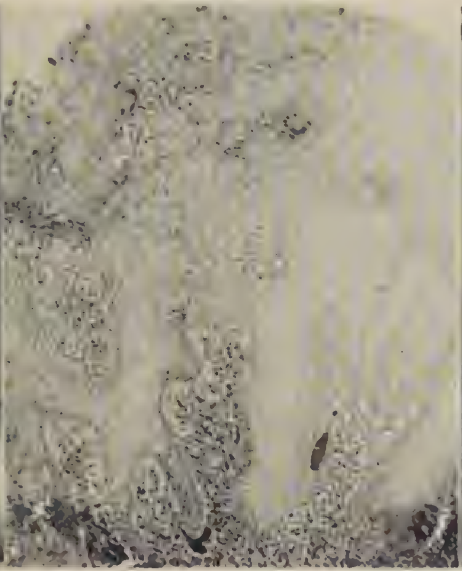


Foreign body granulomatous reaction and fibrosis in nasal mucous membrane incited by oil droplets (injected). x 125.

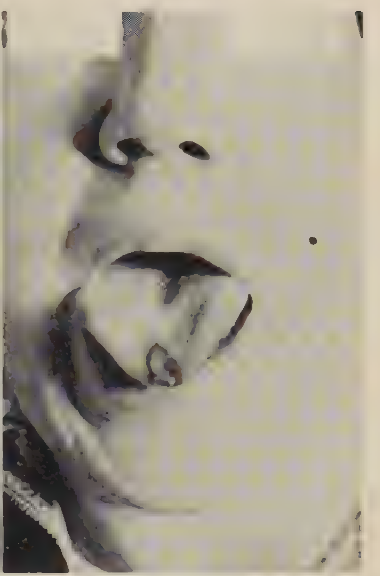
SYPHILIS



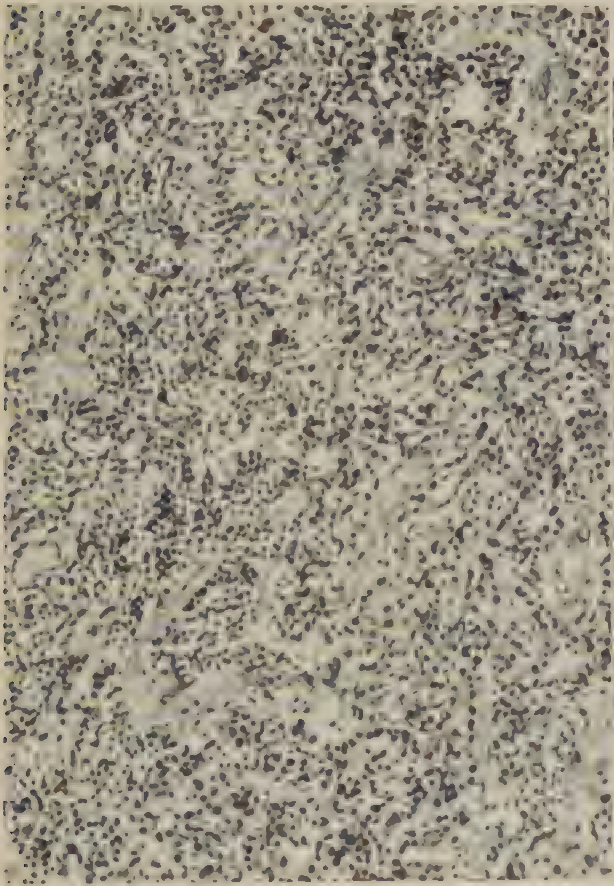
Chancre: Lip: Circumscribed, indurated, superficially ulcerated lesion, resembling carcinoma.



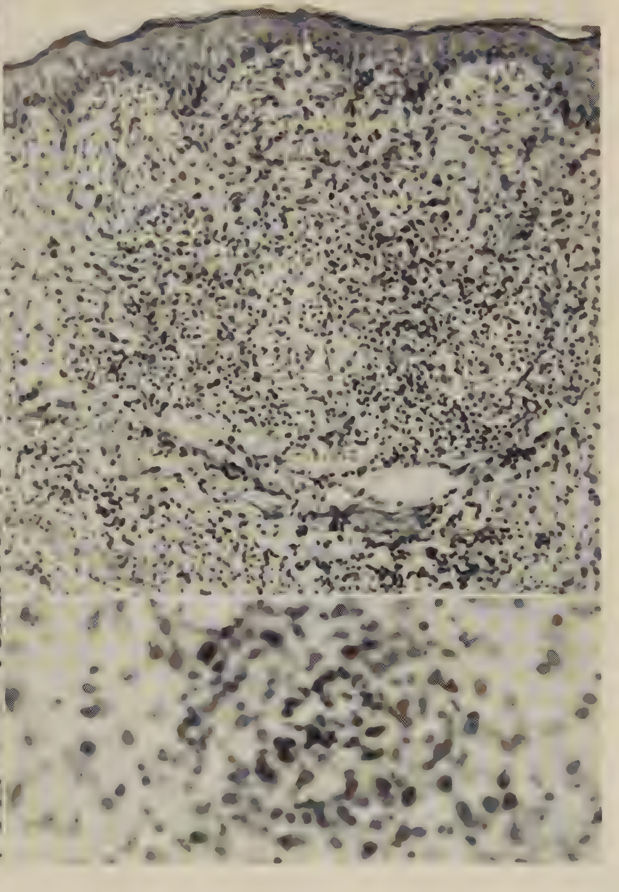
Palate: At margin, hyperplasia of epithelium. Dense subepithelial cellular infiltration.



Tongue: Sharply defined, slightly elevated, indurated lesion.



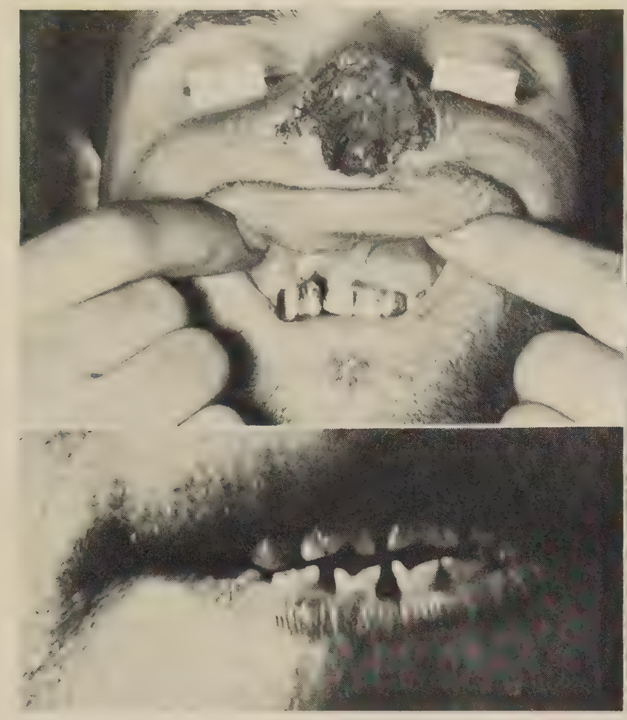
Chancre: Dense exudate of plasma cells and lymphocytes and vessels thickened by endothelial cell proliferation. Prominent budding of capillary vessels. x 210.



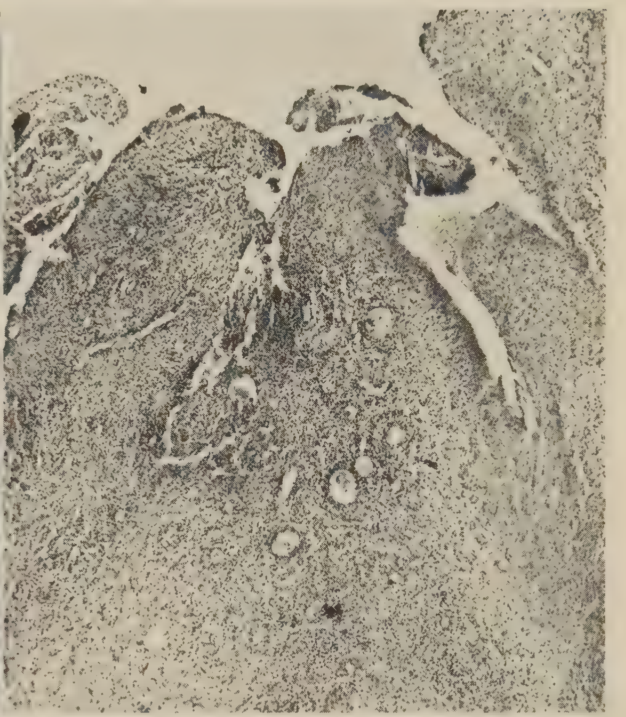
Secondary skin lesion, showing same dense exudate as chancre (upper). x 125.

Blood vessel in chancre almost obliterated by endothelial cell proliferation and exudate in wall (lower). x 300.

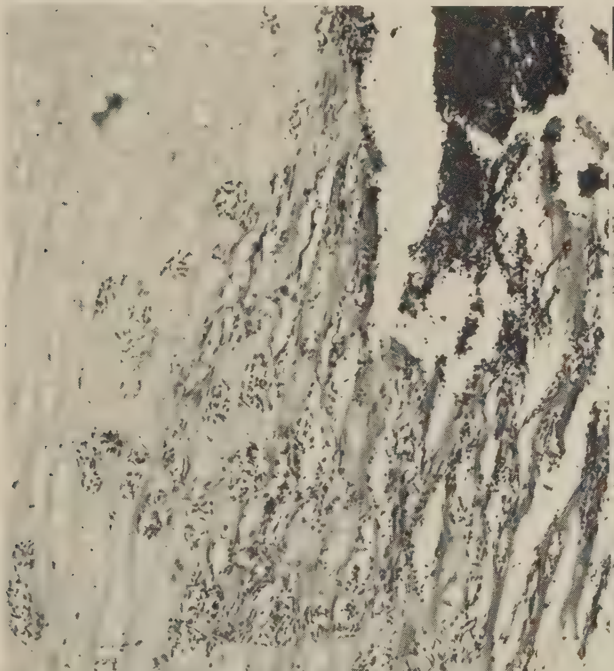
SYPHILIS



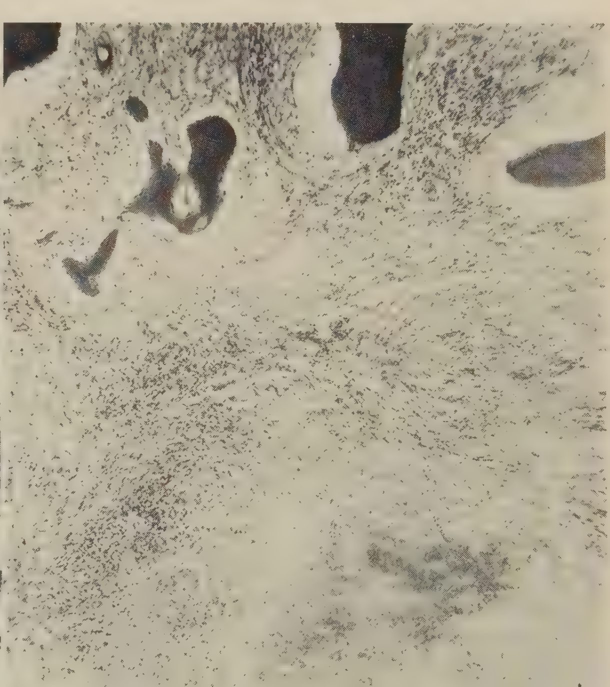
Gummatous destruction of nose and alveolar process of maxilla (upper). **Hutchinson's teeth.** Notched incisors; other dental malformations. Stigma of congenital syphilis (lower).



Tertiary destruction of nasal septum. Ulcerated surface; interstitial infiltrate of lymphocytes, plasma cells and macrophages; obliterative endarteritis; fibrosis. x 62.



Tertiary destruction of septal cartilage. Perichondritis, degeneration and necrosis of cartilage. Same case as upper right. x 70. (W. Putschar, Charleston, W. Va.)



Gummatous osteomyelitis. Bone trabeculae replaced by gumma (at bottom), surrounding vascularized granulomatous inflammation, and fibrosis. x 50.

CHAPTER 3

PIGMENTATION AND DEGENERATION

PIGMENTATION

Pathologic pigmentations are of two general classes: endogenous, from the deposit of pigments formed within the body, of which there are four major sources: blood, lipids, bile, and melanoblasts; and exogenous, from pigments introduced from without, silver and tattooing, for example.

Blood pigments are of two types. The iron-containing element HEMOSIDERIN, the commoner one, is frequently a feature in inflammatory processes where there has been hemorrhage. It is largely responsible for the pigmentation of bruises and the general pigmentation in hemochromatosis. It is readily identifiable by the Prussian-blue reaction to special stains. HEMATOIDIN, the iron-free fraction of hemoglobin, is found occasionally as crystals in hemorrhages and infarcts that are isolated from normal phagocytosis.

The fats and lipids furnish **lipochrome.** This gives the yellow color to the xanthomatoses and to elastic tissue.

The bile pigments do not concern us here.

Melanin is a product of specialized epithelial cells (melanoblasts) normally situated in the basal layer of the skin, choroid of the eye, less noticeably in the mucosa of the large intestine and in the leptomeninges. Melanosis occurs as a general condition in Addison's disease, and as the result of certain drug intoxications, for example, arsenic and atabrine.

Localized melanosis is exemplified in certain skin lesions, freckles, café au lait spots in von Recklinghausen's disease, and is of more serious import in tumors of the melanoblast, the nevus and malignant melanoma. These are discussed under tumors of the skin.

Melanin is usually intracellular; but in pathologic conditions, inflammatory or neoplastic, it is liberated into the tissues where it remains as free particles or is taken up by phagocytes and carried to the adjacent lymph nodes. Special stains may be necessary to differentiate melanin from hemosiderin.

OCHRONOSIS is a rare type of melanotic pigmentation but is appropriately included here because it involves cartilages, particularly those of the ears, nasal septum and larynx. It gives to the ears and nose a peculiar bluish color. It is usually associated with alcaptonuria, i.e., urine that turns black when exposed to the air for a few hours. The condition apparently is an intrinsic disturbance of the metabolism of aromatic compounds. In the past it was seen also as the result of the over-use of phenol in the treatment of open wounds. Melanin is deposited in the cartilaginous matrix and in the denser connective tissue structures such as the sclera.

Of the conditions caused by **exogenous pigments** the most important for our purpose is ARGYRIA resulting from the prolonged use of silver medication, either locally or by ingestion. This is not seen so frequently now as formerly when silver nitrate was used so commonly in the treatment of gastric disorders and when colloidal silver preparations were the vogue in the treatment of upper respiratory conditions. Fine silver particles are deposited especially in the propria of the sweat glands, sebaceous glands, and as free particles in the dermis, but not in the epidermal cells. From the influence of light they become black, giving to the exposed skin a ghastly bluish gray hue. The silver is also deposited in the kidney. The metallic contents of cold cream and medications such as bismuth and mercury are deposited in the same locations and also in the epidermis. The particles are coarser than those of silver.

DEGENERATION

This term, frequently used carelessly to indicate necrosis, should be reserved for cell changes that are reversible. As long as the nucleus is not too seriously involved, the cell can regenerate. The following changes, in order of severity, are classed as degenerations:

Hydrops is the simplest form of the cellular damage. It is the imbibition of water by the cell. The cytoplasm is swollen, pale, and usually vacuolated. This is well illustrated in surface epithelium in milder inflammatory conditions.

Cloudy swelling (albuminous degeneration, parenchymatous degeneration) is the state in which the cell is swollen and the cytoplasm cloudy and granular. It is best seen in the epithelial cells of organs and is the result of milder toxic and metabolic changes. There is a physical if not a chemical change in the proteins of the cytoplasm. The involved organ is increased in size and its cut surface is paler than normal.

Hyalin is a generic term applied to any material in cells or tissues that has a homogeneous or glassy appearance and that takes the acid stain.

Intracellular hyaline degeneration is a slightly more serious phase of protoplasmic damage than either the hydropic or albuminous change. The cell is moderately swollen and contains well defined particles that take the acid stains.

Fibrinoid degeneration is very common and results from the fusion of fibrin or reticulin fibrils, and from the local accumulation of modified intercellular matrix. It is the important feature of such systemic diseases as lupus erythematosus and the other so-called collagen diseases. Another example is von Recklinghausen's hyalin in tuberculous lymph nodes. The striking example in the field of otolaryngology is the so-called amyloid tumor of the larynx.

Zenker's hyalin is a necrosis rather than a degeneration of striped-muscle fibers. The classic example is hyalinization of the abdominal muscles as a complication of typhoid fever, but the change may be seen in other serious infections and in other voluntary muscles.

Colloid is classed among the hyalins although it is a normal product of thyroid acini, but the term is used in referring to masses of hyalin that, although resembling true colloid material, are the result of degenerative or necrotic changes. The term is incorrectly used in certain adenocarcinomas, especially of the colon and breast and even of the nose and sinuses. These are tumors producing large quantities of mucin. "Colloid" in this sense refers to the gross partially jellied-starch character of the material.

Amyloid is really not a direct degeneration of cells or of tissue. It is a newly formed polysaccharide-protein substance that is deposited in characteristic sites but not in cells. Aside from its location it is further distinguishable by its reaction to some of the methyl stains. Because of its ability to absorb Congo red, a clinical test is available for the detection of amyloid. This consists of an intravenous injection of Congo red and a check on its rate of disappearance from the peripheral blood. The commonest clinical form is the secondary amyloid that results from chronic suppurative diseases, particularly tuberculosis and chronic osteomyelitis. In this form the deposits occur predominantly in certain organs, particularly the spleen, liver and kidney. The type that concerns us, however, is primary amyloidosis. In this form, with no apparent cause, amyloid is deposited in various tissues not ordinarily involved in the secondary form. The tongue is most commonly affected and the skin, larynx and lung may be included, or any of these structures may be the site of simple localized tumors. As discussed in the section on the larynx, the true amyloid tumor is rare. The one commonly referred to as amyloid tumor of the larynx is the fibrinoid stage of the laryngeal nodule.

Mucoid degeneration (myxomatous) refers to a change in the intercellular material of connective tissue, particularly in the neoplastic forms—fibromas, fibrosarcomas and neurofibromas—in which there is development of a somewhat viscid fluid that stains faintly with the basic dyes. The cells in such an area are separated by this material; they are usually of a more primitive type than those in other portions of the tumor, and include particularly stellate forms. Tumors that are largely composed of such material are called myxomas, a term that does not indicate the histogenesis of the tumor. The intercellular material in the mixed tumor of salivary-gland type is chemically allied to the real mucoid material of the umbilical cord and to chondromucin.

Mucinous degeneration is not so much a degeneration as it is a hyperactivity of epithelium capable of producing mucin. It is seen in simple form in catarrhal inflammation and in adenomas, and in a more pathologic form in adenocarcinomas, particularly of the large intestine. Such tumors are sometimes called mucinous carcinomas; more commonly but incorrectly, colloid carcinomas. The material here is usually mucin and can be identified by special stains. The material in connective tissue myxomas does not so respond.

CALCIFICATION

Lime salts are commonly deposited in necrotic tissues, particularly in tuberculosis, in fat necrosis, and at times in the necrotic portions of tumors. Deposits in the membrana tympani are common. More generalized deposits of calcium result from alterations in its metabolism from severe kidney damage in the young—renal rickets, and from vitamin and hormonal deficiencies—rickets, osteomalacia, osteitis fibrosa cystica, and in metastatic calcification. The rare foci of calcification seen especially in the soft tissues of the digits are of unknown etiology.

OSSIFICATION

The formation of bone in situations where it normally does not occur is somewhat associated with pathologic calcification. When it occurs as the result of chronic inflammatory processes, the fibroblasts taking part in the repair assume an osteogenic property and can form true bone, including marrow. Common sites for ectopic ossifications are the larger muscular arteries (Mönckeberg's arteriosclerosis), the eye in phthisis bulbi, and injured skeletal muscles (myositis ossificans). Occasionally the cartilages of the ear and frequently those of the larynx undergo ossification. The presence of cartilage and bone in the tonsil and its capsule is discussed in the section on the tonsil.

Fowler calls attention to the point that both ossification and calcification occur where an area of good capillary circulation adjoins an area having poor circulation. This may be applicable to the genesis of otosclerotic changes.

Mesenchymal tumors not necessarily arising from bone or cartilage may demonstrate the osteogenic potential. Such a tumor occurring in the scalp is included among the illustrations of mesenchymal tumors.

ATROPHY

The loss in bulk of a tissue, organ, or cell is called atrophy in contrast to hypoplasia which refers to the failure of a tissue or an organ to develop to its normal proportions. Atrophy results from a variety of circumstances: lack of proper nutrition, interference with the local blood or nerve supply, disuse, and, most important for our purposes, pressure. Atrophy will be met with in a variety of situations throughout the otolaryngic field. This phenomenon is particularly striking when soft masses such as expanding tumors impinge on bone, resulting in osteoclastic absorption of the bone added to the consequences of interference with the blood supply. A striking example is the persistent pressure effect of the otherwise simple lesion, cholesteatoma. Another example is the atrophy of individual tissue cells and blood vessels in the fibrosing phase of inflammation.

HYPERTROPHY AND HYPERPLASIA

These two terms are frequently confused. HYPERTROPHY, in contrast to atrophy, is an increase in bulk without an increase in the number of individual elements, for example, the increase in size of individual muscle fibers in response to increased activity.

HYPERPLASIA, on the other hand, is an increase in the individual elements in a mass, as in hyperplasia of the squamous epithelium in association with chronic ulcerative lesions. The term hypertrophied tonsils, therefore, is not strictly correct because the increase in size is due to an increase in the number of secondary lymphatic follicles and of individual cells. It is difficult at times to differentiate hyperplasia from a neoplastic proliferation of individual cells of a part. Hyperplasia is not possible of all tissue; there is no hyperplasia of normal nerve cells, for example.

SPECIAL HISTOLOGIC STAINS

HEMOSIDERIN

Hematoxylin-Eosin

Pigment brown.
x175

Gomori's Iron Reaction

Pigment blue.
x175

STRIATED MUSCLE FIBERS IN MESENCHYMOMA

Hematoxylin-Eosin

Striations
barely visible.
x500

Phosphotungstic Acid Hematoxylin (PTAH)

Striations
clearly defined.
x500

Masson Trichrome Stain

Smooth and striated muscle, red.
Collagenous tissue, blue.
Erythrocytes, red.
Nuclei, brown to black.
x75

Weigert's Resorcin Fuchsin Elastica Stain

Elastic fibers, black.
x150

Crystal Violet Stain for Amyloid

Stained
Amyloid,
Purplish red.
Hyalin and other
tissues, blue.
x100

Crystal Violet Stain for Amyloid

Strongly positive
focus.
x240

MUCOUS CELL ADENOCARCINOMA

Hematoxylin-Eosin

x500

Mayer's Mucicarmine

Mucicarminophilic material,
pink-red.
x500

Hotchkiss-McManus (Periodic Acid-Schiff Reaction)

x500

TUBERCULOSIS LUNG

Hematoxylin-Eosin

No organisms
stained.
x540

Kinyoun's Carbol Fuchsin

Numerous acid-
fast organisms,
red.
x540

Kinyoun's Carbol Fuchsin

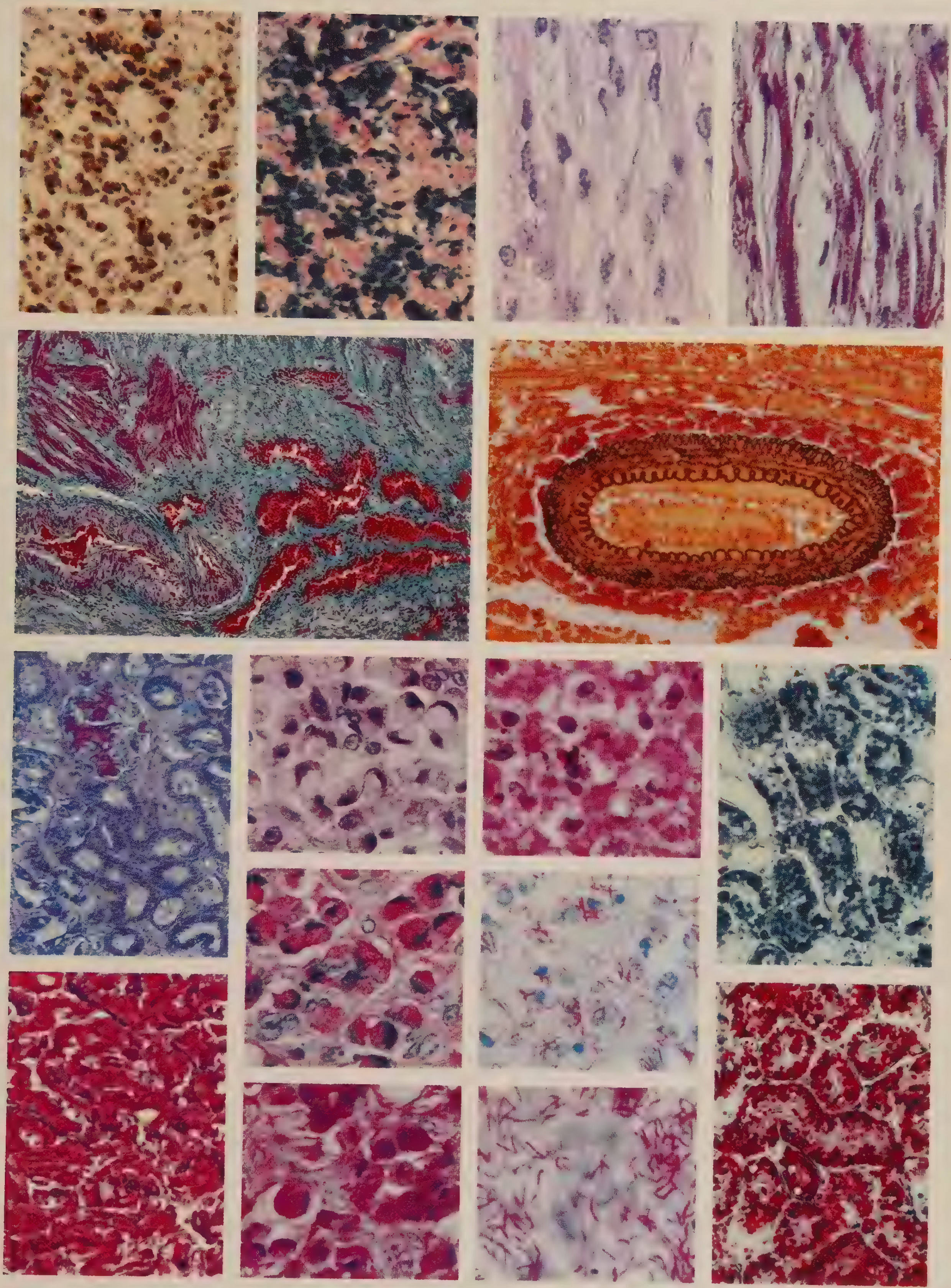
x1260

Formol Sudan Black (Baker)

Lipids, black.
x175

Oil Red O

Lipids,
Orange to red.
x175



CHAPTER 4

NECROSIS AND VASCULAR LESIONS

Necrosis.—The death of restricted portions of tissue in the living body is called necrosis. A few definitions will suffice to recall the various forms that this may take. The death of individual cells is sometimes referred to as NECROBIOSIS, although this term is applied by the dermatologists to the necrosis of collagen as it occurs in rheumatoid arthritis and diabetes.

The necrosis of individual cells occurs in three forms:

LYSIS, in which the cell and the nucleus become swollen with fluid, the nucleus is converted into an ill-defined ring of chromatin or completely disintegrates, and the cytoplasm loses its outline and becomes granular residue. This is not to be confused with hydropic degeneration which is limited to the cytoplasm.

KARYORRHEXIS, in which the nucleus disintegrates into fragments, is the type of necrosis that is characteristic of the necrosis of leukocytes in a purulent inflammation.

PYKNOSIS, in which the nucleus becomes a small concentrated mass of chromatin, is the usual type affecting lymphocytes and plasma cells.

The necrosis affecting larger masses of tissue is also of several types:

COAGULATION NECROSIS is, as the term implies, a fixing of the tissues by coagulation of the protoplasmic elements. The general architecture of the tissue is still more or less retained. Injury by the phenols is a good example of coagulation necrosis.

LIQUEFACTION (COLLIQUATIVE) NECROSIS is the commonest form. The tissues undergo lysis, largely as the result of proteolytic enzymes. Pus is a good example of this form.

CASEATION NECROSIS is so named because of the gross cheesy character of the necrotic material. The tissue undergoes complete disorganization and even the nuclear fragments disappear, but the fluid content seen in other forms of necrosis is lacking. This form is typified by the caseation in tuberculosis.

FAT NECROSIS may result from either of two processes: *a.* digestion by escaped pancreatic juice, and *b.* rupture of fat cells, usually by trauma. The released fat undergoes change to fatty acids and soaps that act as foreign bodies inciting granulomatous inflammation, with formation of foreign body giant cells.

Thrombosis.—Coagulation of blood in a vessel lumen, i.e., thrombosis, is practically always secondary to injury to the vessel wall, especially to its endothelial lining, by trauma, infection, or toxic action. It is a most important process in inflammatory lesions because occlusion of vessels frequently contributes to the extension of tissue destruction by infarction, or by interference with the blood supply with consequent tissue anoxia. When the thrombus is the result of direct infection of the vessel wall, the thrombus itself may be infected and the process is called thrombophlebitis or thromboarteritis. The infection may be further disseminated directly by extension of the thrombus along the vessels to more distant parts or by metastasis through emboli which break from the thrombus.

The thrombus consists of platelets, fibrin and enmeshed blood cells in varying proportions. Organization of the thrombus begins early and under favorable circumstances proceeds to complete replacement of the blood clot by connective tissue and blood vessels. These newly formed vessels become so distributed as to create channels through the clot, thus re-establishing a portion of the flow of blood. This process is canalization of the thrombus.

THROMBOPHLEBITIS is of particular importance to the otolaryngologist because of the likelihood of infection and thrombosis of the important venous channels in the dura and the frequency of osteomyelitis as a complication of sinusitis. Ludwig's angina is another clinical entity determined by the extent of the secondary thrombophlebitis.

LUDWIG'S ANGINA is a definite clinical entity although the term has been rather loosely used to include any cellulitis of the tissues of the floor of the mouth and neck. It is characterized by woody induration. It usually begins in the floor of the mouth and characteristically involves the tongue, although it may extend into the neck. *Streptococcus hemolyticus,* the organism most commonly implicated, probably gains access to the areolar tissues in the floor of the mouth from infected teeth, tonsils, or salivary glands. Ludwig's angina usually occurs in young adults, with high fever and severe leukocytosis as symptoms. The process spreads rapidly, characteristically involving only one side of the neck and producing a board-like swelling. When fully developed it is accompanied by great pain.

There is little, if any, actual suppuration. The process spreads as a phlegmon and also as thrombophlebitis which is the striking feature histologically. The affected tissues are undergoing necrosis and there is a widespread heavy exudate, predominantly of the small mononuclear type but also containing polymorphonuclear neutrophils, including collections forming micro-abscesses.

The condition is serious, for if it cannot be arrested in its early stages by sulfonamides and antibiotics, ordinary surgical drainage does not suffice to arrest the spread of the infection, and death usually results from suffocation or septicemia.

The illustrations in the following plates were made from material from a 57-year-old woman who had cellulitis in her neck for several days following a tooth infection. In spite of tracheotomy performed to relieve the severe dyspnea, the patient died in a few days. In this instance the thrombophlebitis extended throughout the entire tongue, which explained the futility of the conservative operative procedure.

Death of larger portions of tissue are on a vascular basis.

INFARCTION is the death of a well-defined segment of tissue resulting from the occlusion of a terminal vessel, usually of an organ. This results in hemorrhage into and necrosis of the included parenchyma. The early stage is the hemorrhagic infarct, which later becomes an anemic infarct from hemolysis and disappearance of the blood pigments, and eventually a scar. Infarcts in the brain may, however, be originally anemic. These are varying sized areas of liquefaction of cerebral tissue without the usual hemorrhage of an infarct forming elsewhere.

Gangrene.—Infarction combined with putrefaction is called gangrene. Four types are recognized:

DRY GANGRENE, the usual form affecting extremities from occlusion of arteries, as in diabetic arteriosclerosis and in thromboangiitis obliterans.

MOIST GANGRENE, involving tissues that are more readily invaded by saprophytes and putrefactive organisms. This is seen particularly in the lungs, intestines and mouth.

GAS GANGRENE, resulting from invasion of necrotic tissue by gas-forming bacteria of the Welch group.

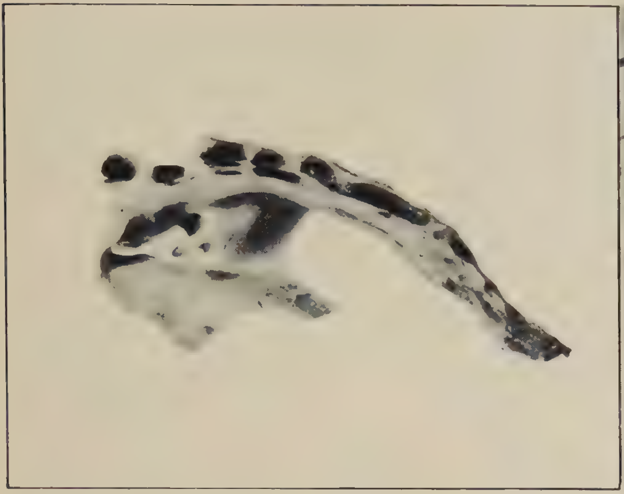
DECUBITUS ULCER (bed sore), resulting from pressure on surface areas during debilitating disease or from vascular damage in certain acute infections, for example, typhus fever, a rickettsial disease.

There are several other clinical examples of gangrene the pathogenesis of which is difficult to explain. Pudendal gangrene, more common in the female, results in the destruction of the external genitalia and the perineum. It develops in older individuals, usually as a complication of a sustained debilitating disease. Gangrene of the soft tissues of the mouth and face is another; and the third, fortunately very rare, involves the median tissues of the face. In a few months, despite treatment of any kind, there is destruction of nose, lips and cheeks, and death from toxemia follows.

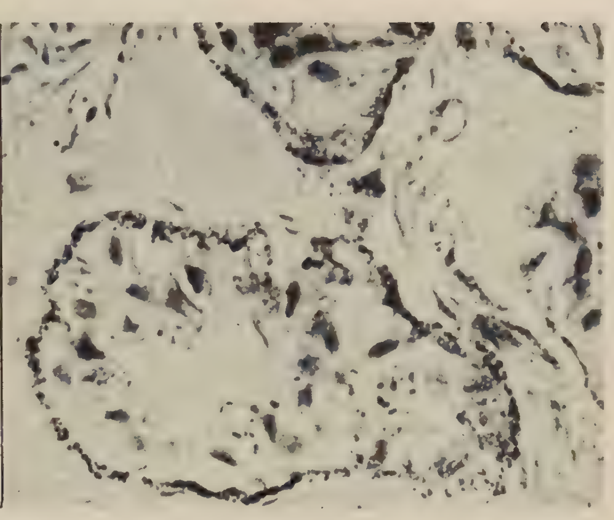
STOMATITIS GANGRENOSA (NOMA) is a rare but very serious clinical entity, usually of children but occasionally of adults. In its full-blown state it consists of gangrene of the cheek involving both mucosal and skin portions. It probably begins as a bacterial infection, with the gangrene secondary to thromboangiitis. The spirofusiform organisms of Vincent's disease are practically always present in the lesion but are probably only contaminants. The initial lesion is a small painful papule in the buccal or gingival mucosa, which becomes ulcerated. The tissues of the cheek gradually become greatly swollen and indurated, then an area of redness appears which later becomes a black necrotic plug. Sloughing of the necrotic tissue leaves a perforation into the mouth. Peripheral extension of the cellulitis and necrosis usually proceed to septicemia and death. Thus if the lesion is not completely removed surgically in the early stages, it is practically always fatal.

The illustrations of noma in the following plates are from a case contributed by Trible and Dick of Washington. This patient was a woman 35 years of age, with progressive anemia. The gum became red, and pain through the face, ear and neck became increasingly severe. A month later the redness appeared on the cheek and in a few days a necrotic plug sloughed out leaving a perforation. Necrosis and cellulitis spread rapidly and the patient died with streptococcal septicemia.

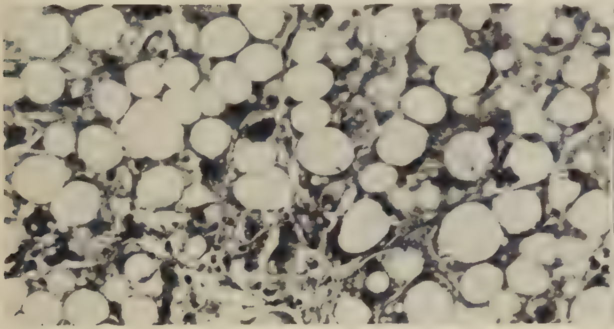
There is also a clinical picture of noma as seen in children.



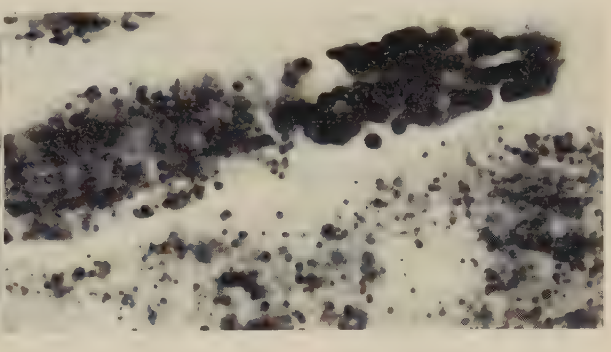
Ochronosis, trachea. Cartilages are black from deposits of melanin.



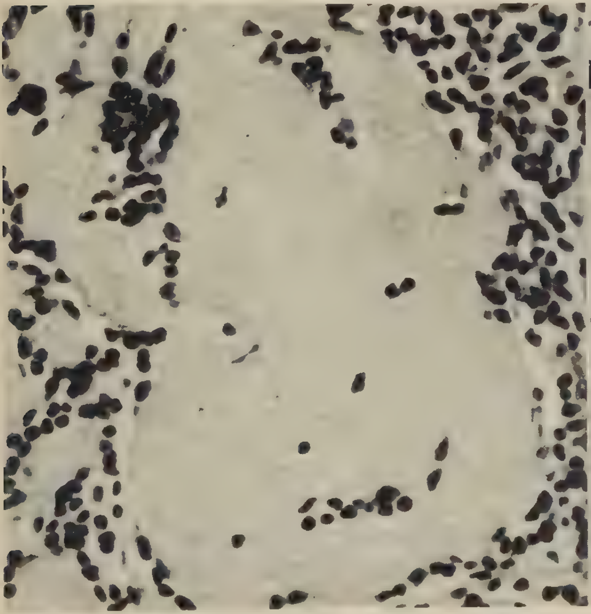
Argyria. Basement membranes of sweat glands are black from the silver. x275.



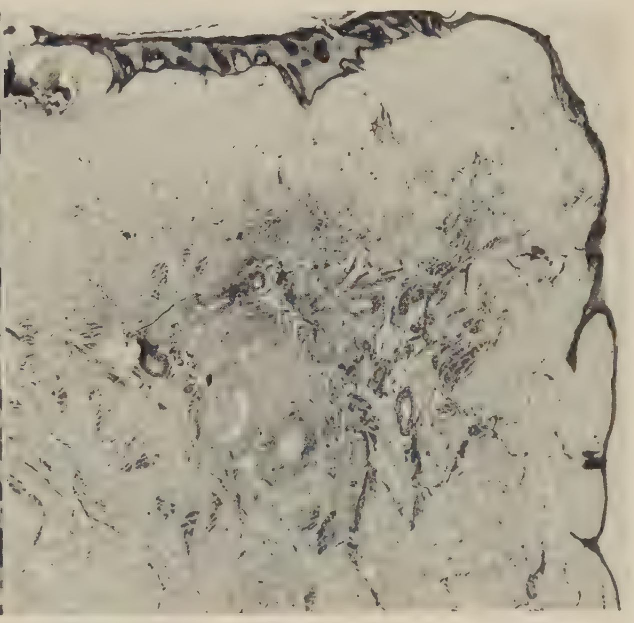
Fatty metamorphosis, liver. Fat in large globules. x145.



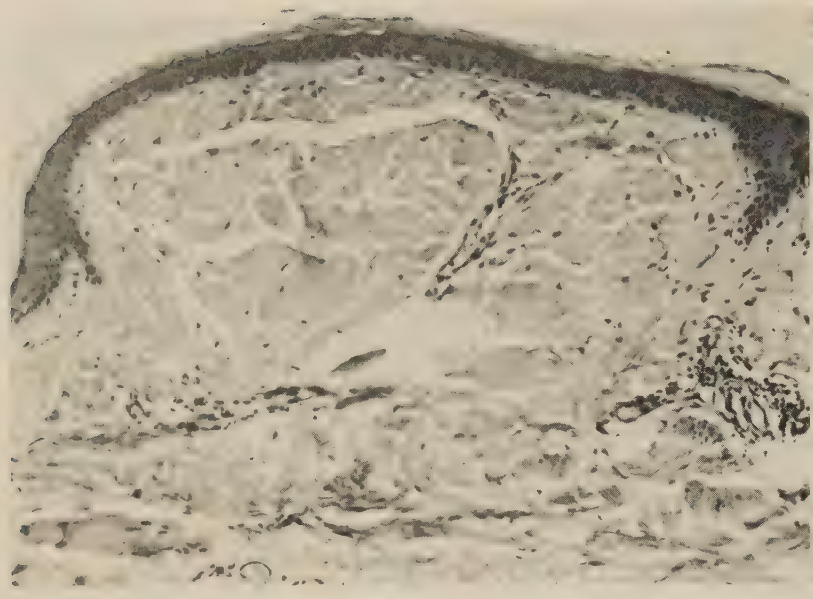
Fatty degeneration, heart muscle. Fat in very fine globules. Osmic acid stain. x422.



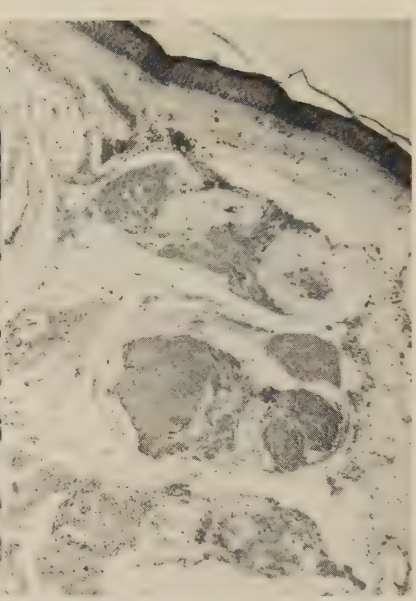
Hyaline degeneration, von Recklinghausen's, in tuberculous lymph node. x400.



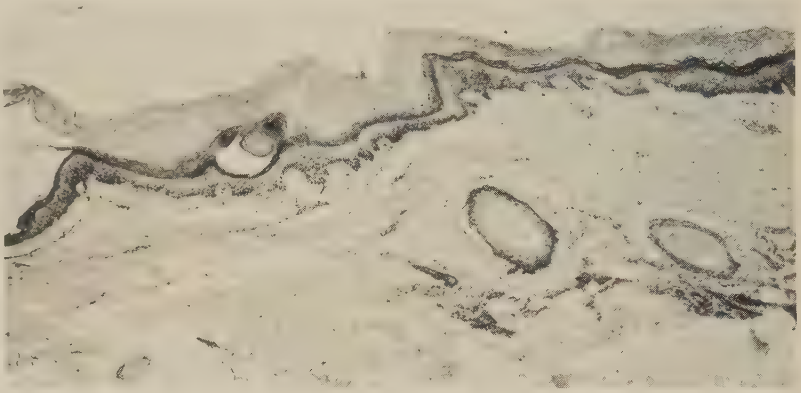
Amyloid, tongue. Vessel walls thickened and muscle fibers separated by the deposit. x558.



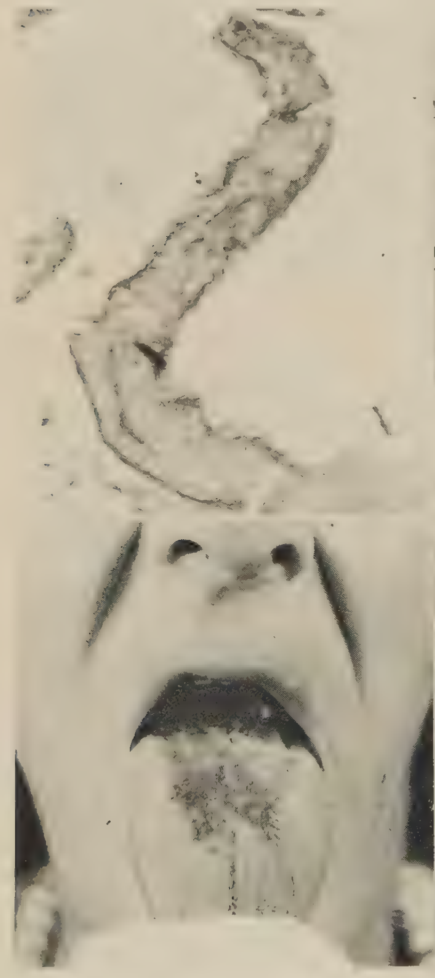
Hyaline degeneration. Colloid milium skin. Subepidermal nodular masses of altered collagen. x 55.



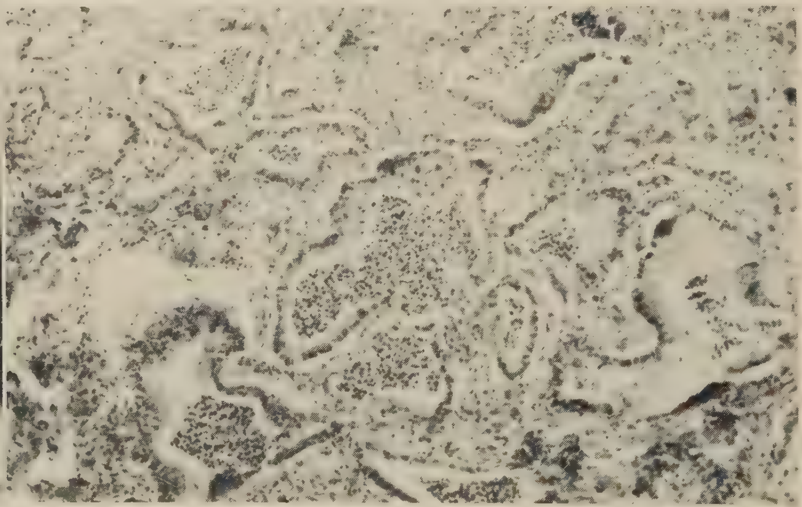
Fibrinoid material in and about vessels in laryngeal nodule. x 35.



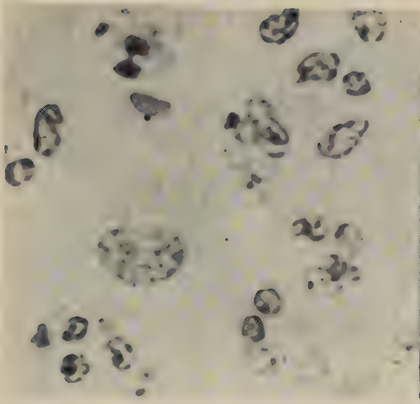
Atrophy of skin in xeroderma pigmentosum. Both epidermis and dermis are reduced in thickness. x 55.



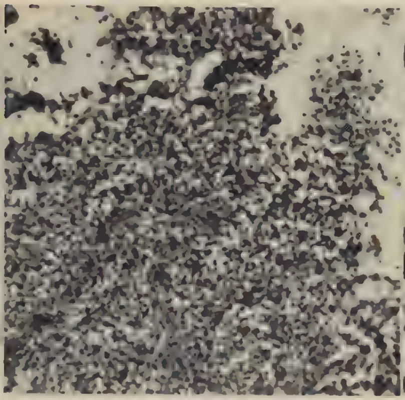
Hypertrophy. Hairy tongue: hypertrophy of filiform papillae. Individual villus. x 40. Clinical appearance below.



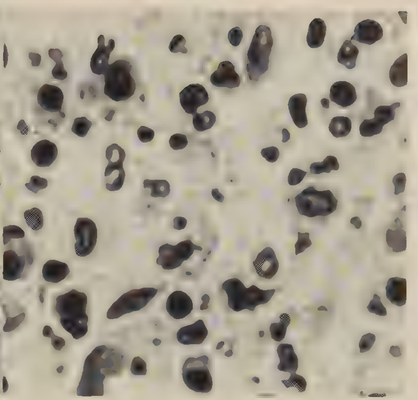
Metaplasia and **Hyperplasia** of bronchiolar epithelium in fibrosed lung. x 250.



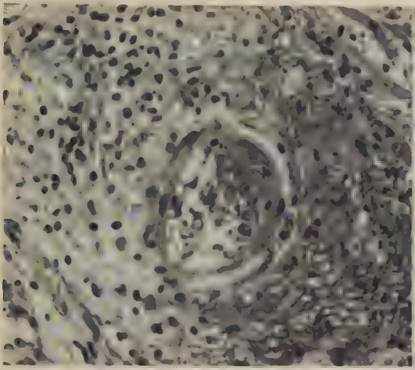
Nuclear necrosis:
Karyolysis, nuclei swollen and hydropic.



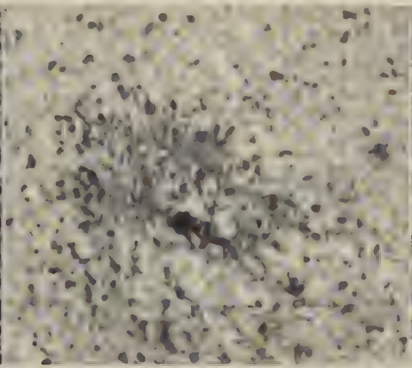
Karyorrhexis, nuclei fragmented. Abscess. x 125.



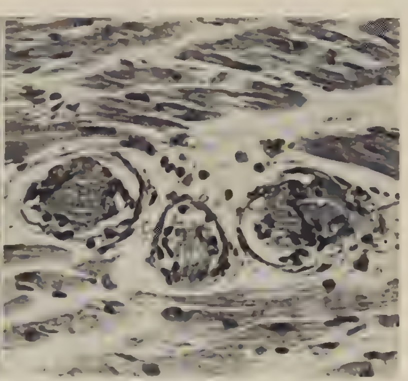
Pyknosis, nuclei of lymphocytes and plasma cells shrunken and dark. x 810.



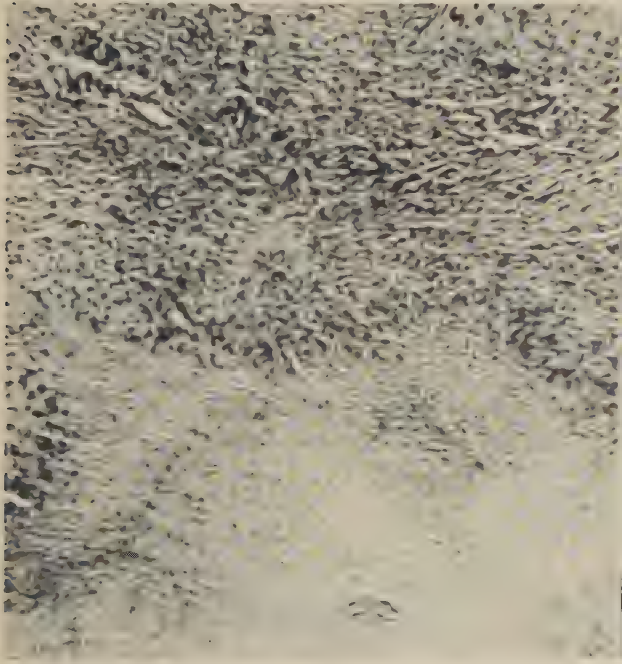
Fibrinoid degeneration of arterial and periarterial collagen, with thrombosis, in epidemic typhus. x 230.



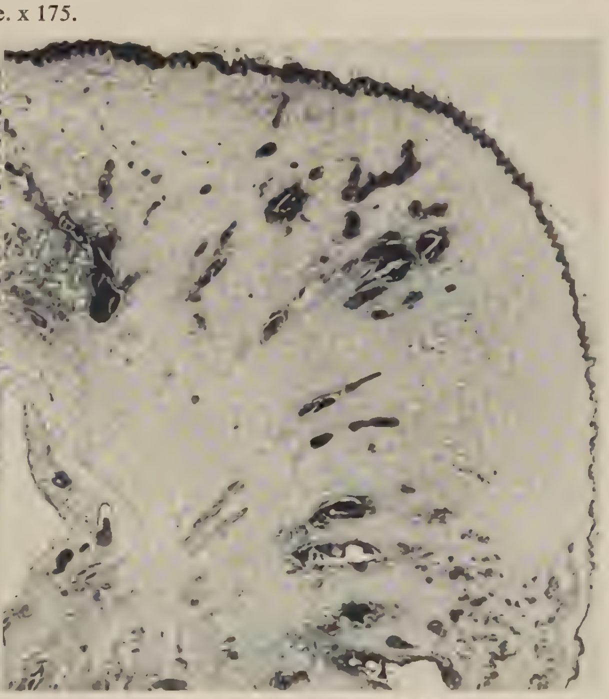
Infarct, white, brain, in Rocky Mountain spotted fever. Necrosis, but no hemorrhage. x 175.



Platelet thrombosis, in heart muscle.

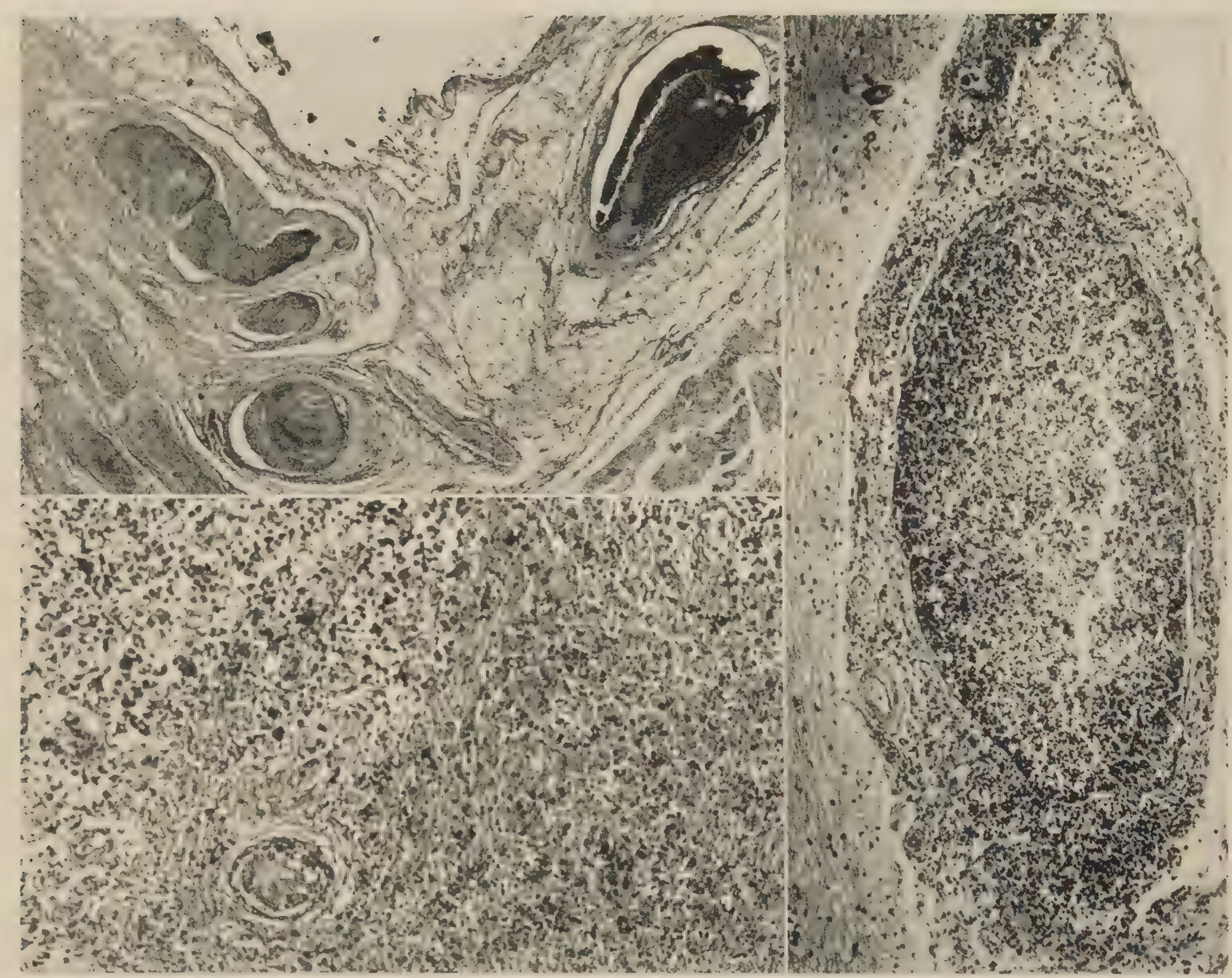


Fibrinoid necrosis of collagen in subcutaneous rheumatic nodule, surrounded by radially arranged mononuclear cells. x 90.

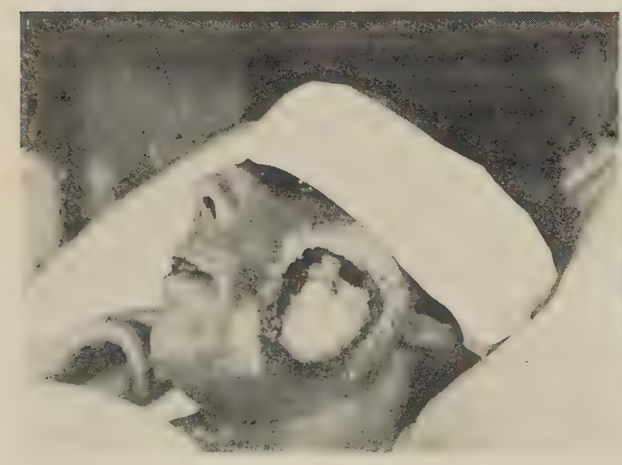


Thrombosis, multiple, tongue, in Ludwig's angina—a phlegmonous inflammation of the floor of the mouth.

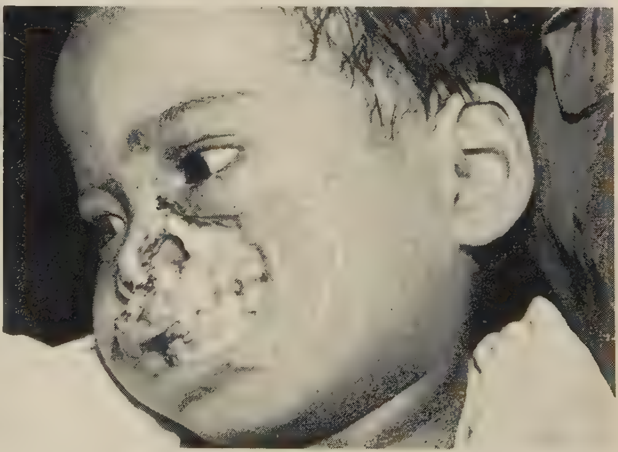
GANGRENE



A. **Thrombosis,** Ludwig's angina. x 15. B. **Thrombosis with necrosis,** lymph node. x 145. C. **Thrombophlebitis,** meninges, following tooth extraction. Exudate in vessel wall. x 100.



Noma. Gangrene of full thickness of cheek in adult, fatal.



Noma, gangrenous stomatitis, healing.

CHAPTER 5

DEFICIENCY AND BLOOD DISEASES

Since discovery of the vitamins and the etiologic importance of vitamin deficiencies in the specific clinical entities, scurvy, sprue, beri-beri and pellagra, these diseases are less often seen in their classic form. Today we are faced with the subtle and less readily recognizable symptoms of deficiency, usually of one or more elements of the vitamin B complex and of vitamin A. Since these effects are chiefly in the skin and mucosae, they are of practical importance to the specialist concerned with these tissues.

Vitamin A is a fat-soluble vitamin which seems to be concerned particularly with maintaining the structure and function of certain types of epithelium and with the production of visual purple. The manifestations of deficiency are seen chiefly in the epithelium of the salivary glands, respiratory tract, skin, and conjunctiva, and are characterized by metaplasia of epithelium to the squamous type. Such change in the epithelium of the trachea and bronchi may lead to serious interference with function. Generalized hyperkeratosis of the skin causes its clinical roughness and scaling; keratosis of the follicles is particularly prominent, and the conjunctiva becomes dry and scaly (xerophthalmia), a very serious condition that may lead to blindness.

Vitamin B deficiency in the **thiamine** component is responsible for BERIBERI, manifested clinically by serious cardiac damage, peripheral edema and nerve changes. It is now generally believed that the multiple neuritis of alcoholism results from the inadequacy of diet rather than directly from the alcohol.

Deficiency of the **riboflavin** component of vitamin B produces striking clinical manifestations because of its effect on the mucosa of the lips, tongue and mouth. The vermilion portion of the lips is red and scaly, the corners of the mouth are characteristically fissured (CHEILOSIS), and the tongue is magenta red but not as brilliant as the tongue in pellagra. The mucosal changes are also striking in SPRUE, in which complex, in addition to stomatitis and glossitis, there is involvement of the gastrointestinal mucosa and finally severe macrocytic anemia.

Niacin deficiency is a prominent feature in the etiology of PELLAGRA. This disease is of interest to the otolaryngologist because, in addition to the scaly, fissured skin lesions of the hands and neck, the mucous membranes are involved. The membranes of the mouth, including the tongue, become swollen, red, and ulcerated. The oral lesions resemble somewhat those of aphthous stomatitis.

The histologic picture in pellagra is not diagnostic, but the epithelium of both skin and mucosa in the early active stages shows spotty acanthosis, hyperkeratosis, and even dyskeratosis, with some liquefaction necrosis of basal cells and ulceration. The papillary layer of the dermis is edematous, the blood vessels dilated and surrounded by a moderate amount of exudate, chiefly lymphocytes. In the later stages, there is atrophy of both epithelium and dermis on a neural basis.

It is very likely that vitamin B deficiency is a factor in the Plummer-Vinson syndrome discussed under tumors of the esophagus.

Vitamin C (ascorbic acid) deficiency is responsible for SCURVY. This deficiency is characterized by hemorrhages not only into the gums, joints, and periosteum but also into the skin and muscles. Vitamin C is a factor in the physiologic processes of the intercullar substances, especially collagen and the ground substance of the vascular endothelium, and this accounts for the hemorrhagic manifestations in vitamin C deficiency.

Vitamin D deficiency is responsible for RICKETS and OSTEOMALACIA. This vitamin plays an important role in the metabolism of calcium and phosphorus, hence the striking deformities of bone and cartilage that characterize rickets in young children.

In spite of the serious consequences of the deficiency of an individual vitamin, none is evident in complete starvation. A volunteer studied some years ago by a group that included one of us (A.) at the Carnegie Nutrition Laboratory in Brookline, Mass., during a fast of 31 days, exhibited none of the local changes described. They did occur, however, in prisoners of war who for long periods were on generally deficient diets. An illustration from one of these is included in the following plates.

DISEASE OF THE BLOOD

Agranulocytic Angina (Aplastic Anemia).—Interference with normal hematopoiesis produces this serious local complication of the mouth and pharynx. Agranulocytosis can be produced by a variety of toxins which includes many drugs, particularly those of the class of the amidopyrines. More recently chloromycetin has been implicated. A number of instances of serious and even fatal blood dyscrasias have been reported as following the repeated use of the drug. A similar effect is produced by exposure to massive irradiation. It was one of the serious clinical features of the atomic bomb victims in Hiroshima and Nagasaki. In fact, the oral and pharyngeal changes were used as an indication of the presence of radiation sickness.

The local manifestations of the severe blood dyscrasias usually begin as hyperemia of the surface of the tonsils and of the gum margins. Diffuse congestion and loss of epithelial surface rapidly follow, with the development of a membrane over the reacting parts. In the later stages there is deeper necrosis of the tissues and the overlying membrane becomes dirty gray and necrotic. The blood picture reflects the suppression of hematopoiesis by the striking reduction in granular polymorphonuclear cells. The absence of polymorphonuclear cells in the lesions greatly impairs resistance to infection and this makes possible septicemia and bacteremia. Vincent's organisms can usually be demonstrated in the necrotic areas, but they must not be considered the etiologic agents.

Microscopically, the picture varies with the extent of the necrosis. There is severe edema and replacement of the covering epithelium by a pseudomembrane made up of fibrin and necrotic debris. The necrosis extends into the tissues for varying distances. The striking and almost diagnostic feature is the absence of polymorphonuclear leukocytes in the presence of such a fulminant lesion. The exudate is of the mononuclear type, predominantly lymphocytic, with a few plasma cells and varying numbers of large mononuclear phagocytes. If the process has persisted for several days there will be proliferation of young blood vessels and fibroblasts. The endothelium of the blood vessels is usually swollen.

A somewhat similar picture results from leukemia, particularly the acute forms. Local infections, however, such as Vincent's angina and septicemia, are to be eliminated by the clinical history and a study of the blood and bone marrow.

Leukemia.—It is not necessary to go into the details of the histogenesis, pathology, and clinical aspects of the specific leukemias and anemias, but it is pertinent to outline the local manifestations of these diseases. Frequently the specialist—the dentist, the dermatologist or the otolaryngologist—is the first to be consulted because of the local manifestations of these diseases in their early stages. It is vital that the significance of bleeding gums, ulcerated fauces, and unusual hemorrhage following tooth extraction be constantly kept in mind. The importance of a blood study before an operative procedure, especially in children, becomes obvious. Patients suffering from acute leukemia are poor operative risks.

The lymphatic elements of the fauces and pharynx frequently share in the neoplastic hyperplasia, particularly in the lymphatic and monocytic forms of leukemia. In addition there may be a diffuse deposit of neoplastic cells in the mucosa, particularly in the gingivae. In the acute forms, petechiae on and frank hemorrhages from many of the mucosal surfaces are usual manifestations. Stomatitis and pharyngitis with ulcerations are not infrequently the initial symptoms. The severe reactions in the mouth and throat are associated with both the acute forms of the leukemias and the terminal acute exacerbations of the chronic forms.

Leukemic infiltration occasionally occurs in the middle or inner ear. Such a case is illustrated in the following plates and in the division on the ear. In this instance the otologist was the first to make the diagnosis.

Microscopically, enlargement of the lymphatic tissue elements is due to invasion by the tumor cells. The common feature in all types of leukemia is the partial or complete obliteration of the normal architecture of the secondary lymphatic follicles, but the cell characteristics will vary with the type of leukemia. It is not possible to tell from a microscopic examination of tissue whether one is dealing with a tumor of the lymphatic tissue, lymphosarcoma, for example, or with leukemia, unless in the section there are blood vessels containing enough blood to determine the presence or absence of leukemia.

The lesions in the tissues other than the lymphatic elements vary with the extent of necrosis and the secondary inflammatory reaction. It is not unusual in leukemia for neoplastic cells to be included in the exudate, and from these it may be possible to determine the type of the leukemia.

Mycosis Fungoides (Granuloma Fungoides).—This is not strictly speaking a blood disease but is rather an ectopic lymphoma. In the terminal granuloma state (a poor term, for the lesions have no resemblance to a granulomatous inflammation), there is an accumulation of malignant lymphoma-type cells in the skin. At times the picture is like Hodgkin's disease and is so designated by some. The prefix "mycosis" has been used because of the mushroom-like appearance of some of the tumors in the advanced stage of the disease.

The disease is more common in the male and in adult life and occurs in three clinical stages. The first, or premycotic phase, may begin as pruritus that may persist for years before any rash develops. The rash appears in a wide variety of forms. It is usually generalized and simulates eczema, psoriasis, or even the more serious exfoliative dermatitis. Itching is a pronounced symptom throughout this phase. Sooner or later the second or infiltrative phase develops, during which the varicolored nodules or less well-defined irregular areas of thickening make their appearance. Examination of the skin in this phase will show the lesions to be the result of the accumulation of cells that include lymphocytes and reticulo-endothelial cells having neoplastic characteristics. The epidermis is usually acanthotic and may show the classic feature, the Pautrier abscess in the malpighian layer. This lesion is made up of liquefaction necrosis and accumulation of lymphocytes. Even in the preliminary stage of nonspecific dermatitis, neoplastic cells may be present.

In the terminal phase, the neoplastic cells become more concentrated and more consistently of the reticulum cell type, including giant cell forms.

The peripheral blood picture is usually not altered, but there may be infiltration of organs and tissues other than the skin. The disease is practically always fatal.

Infectious Mononucleosis.—Although not belonging to the category of serious blood disorders so far discussed, infectious mononucleosis should be included here because of its clinical manifestations in the tonsils and cervical lymph nodes.

Infectious mononucleosis (glandular fever) is a clinically protean infection, possibly viral, that affects children and young adults particularly. The commoner symptoms are a low grade fever, malaise, sore throat, and enlargement of lymph nodes, particularly the cervical. The spleen is usually enlarged. The symptoms vary so in character and intensity that the diagnosis is possible only by the blood picture and the demonstration of heterophile antibodies in the blood serum by controlled tests. The course may be acute or long sustained with remittent bouts of fever and sore throat. The disease is rarely fatal, but rupture of the spleen was noted in several instances among military personnel during the last war. The disease is apparently only mildly contagious, but communities become endemic centers.

Atypical large lymphocytes appear in the peripheral blood and are deposited in the lymphatic tissues and, to a smaller extent, in the organs. The illustrations depict this reaction in the spleen, lymph nodes and tonsils. The normal architecture of the tissue is disturbed and the atypical cells are present in varying numbers. Infiltration of the splenic capsule by the atypical cells has been described as the reason for the ruptures of that organ. It is well to restrict the patient's activities to avoid this serious complication.

Pernicious and **aplastic anemias** manifest themselves in the mouth and throat by atrophy of the mucosa which is evidenced by a smooth, shiny surface, and a swollen or fissured tongue. In the aplastic forms a picture similar to that produced by agranulocytosis may be seen, particularly terminally when there is a depression in the development of the cells of the granulocytic series.

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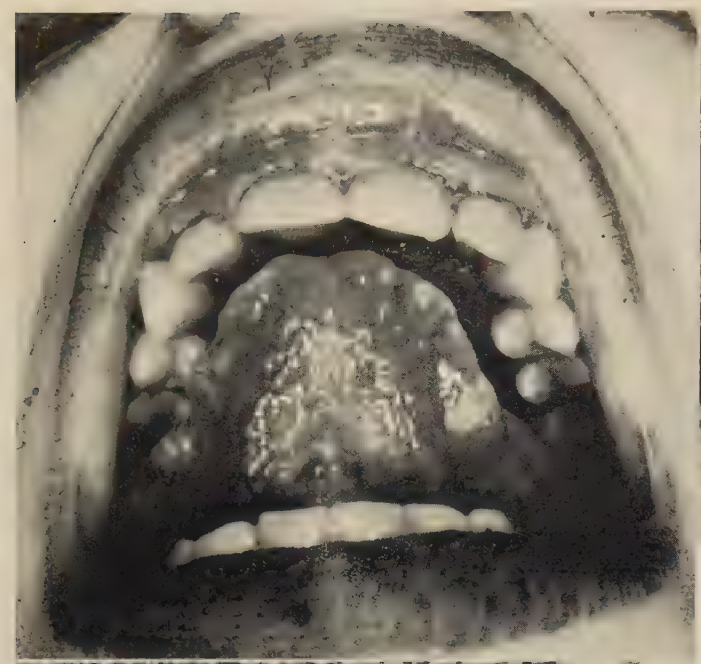
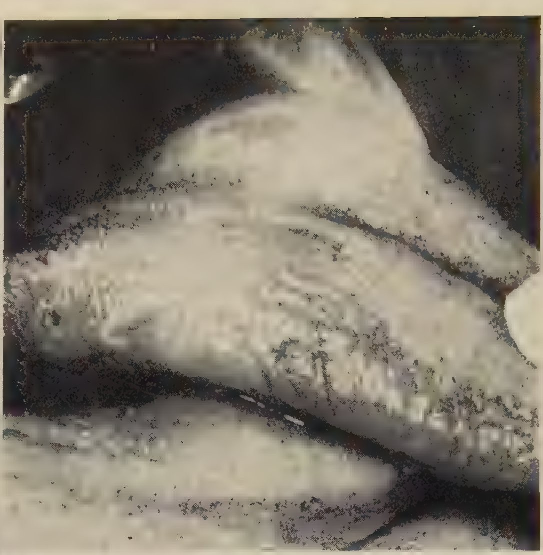
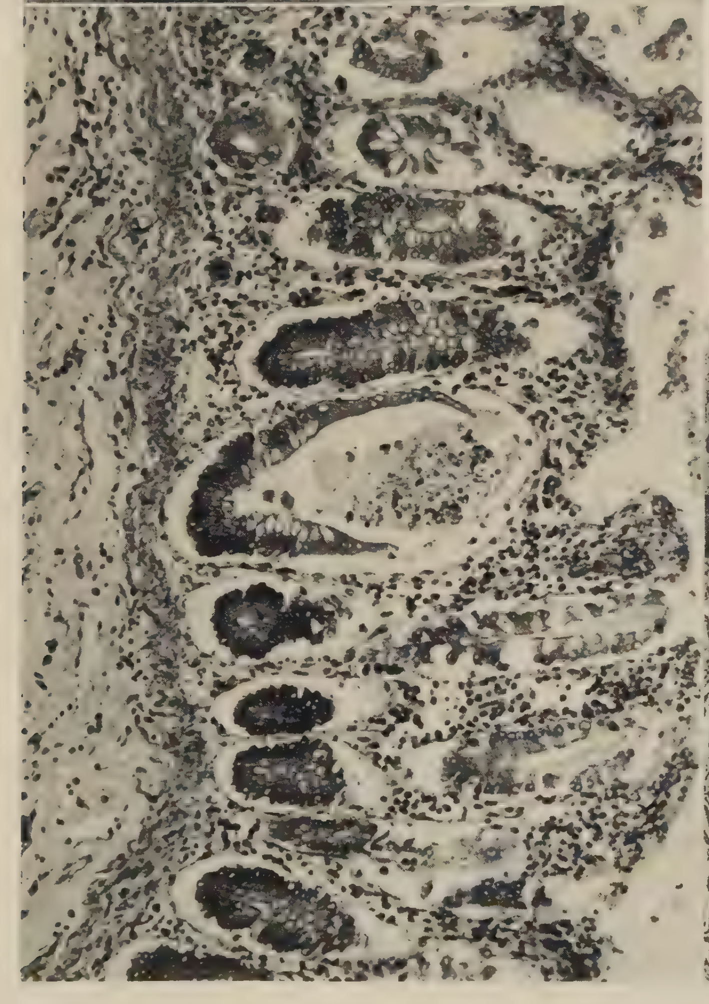
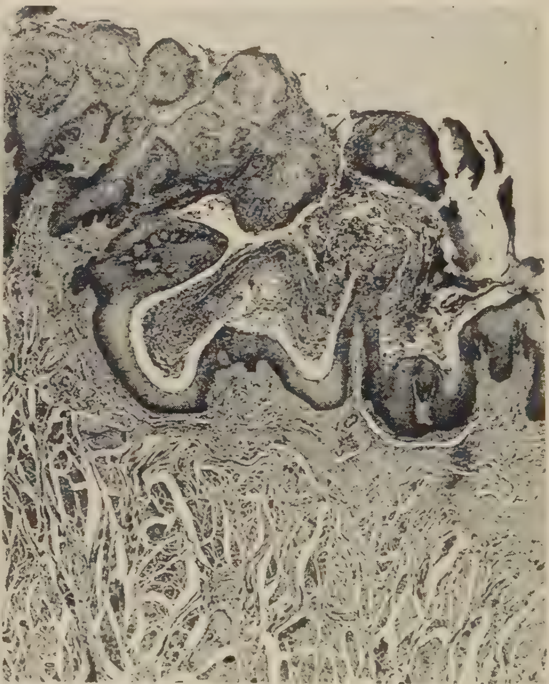


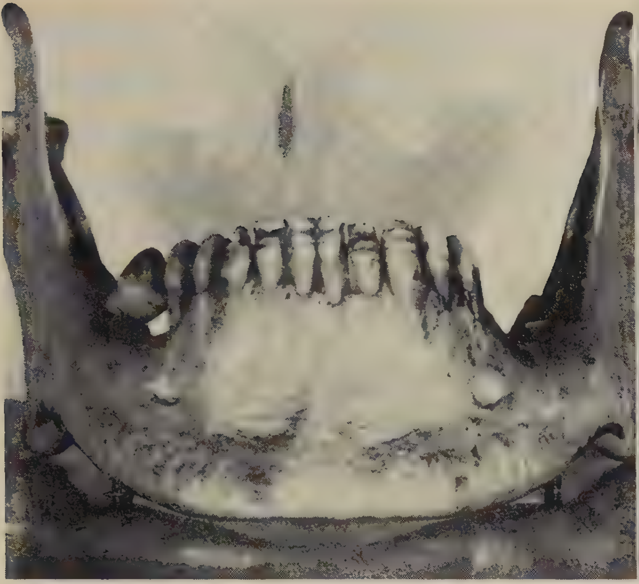


Sprue: A. Gums swollen and red; aphthous patches on tongue. B. Glossitis. Lateral borders of tongue are red, shiny and furrowed. Epithelium is atrophic. C. Colon. Mucosa is infiltrated by mononuclear cells, submucosa is edematous. Note retention cyst. Similar changes may occur in other deficiency diseases. x 160.

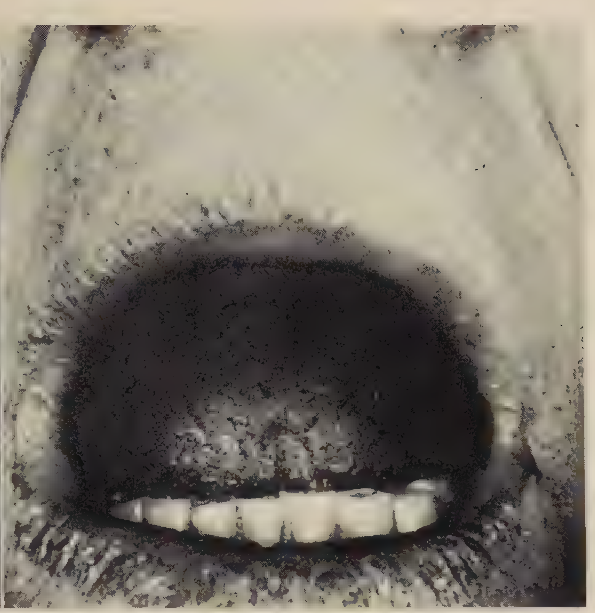


Starvation, tongue (below). Epithelium is keratotic and shows papillary hyperplasia; result of vitamin A deficiency ? x 26.

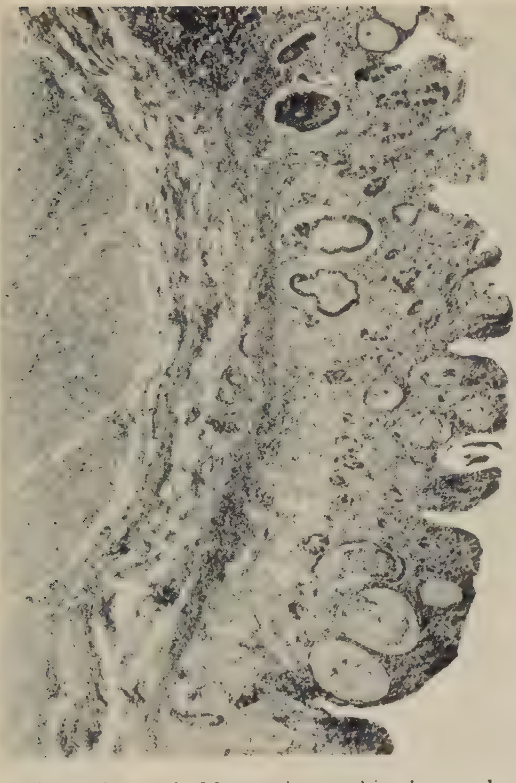




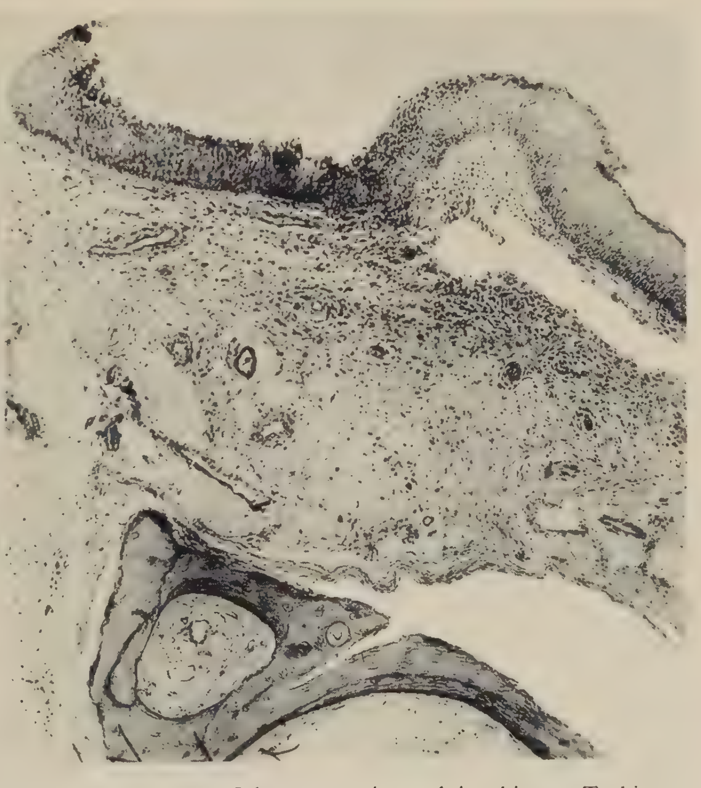
Rickets. Laminated, notched and ringed teeth result from interference with calcification by vitamin D deficiency. Note difference from Hutchinson's teeth. Mandible deformed by faulty ossification.



Pellagra. Cheilitis. Mucosa and skin of lips are dry, wrinkled and cracked. Tip of tongue is swollen, rough and fissured.

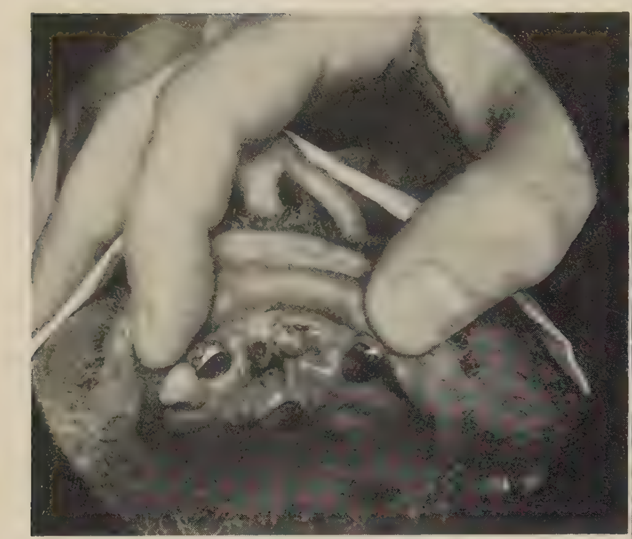


Pellagra. Stomach. Mucosa is atrophic; deeper glands form cysts, as seen in sprue; blood vessels congested. x 40.

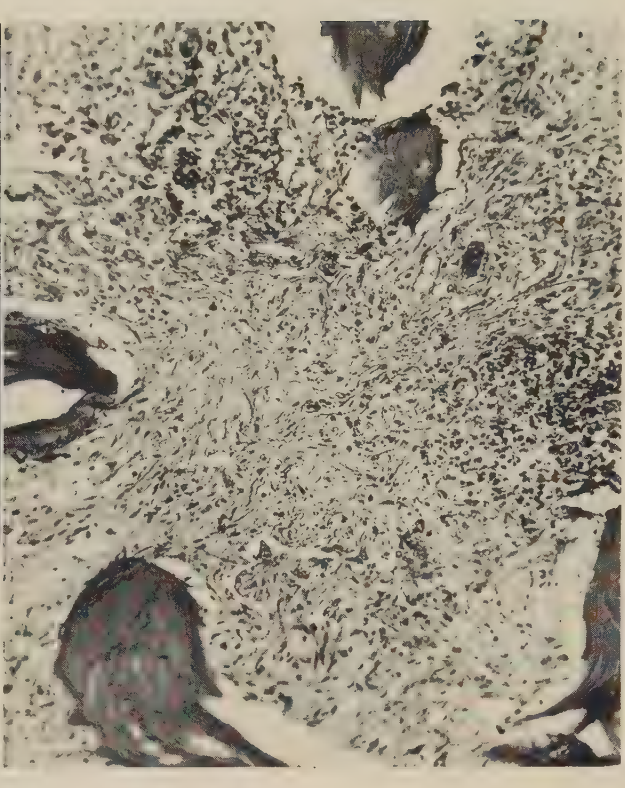


Vitamins A and D deficiency, experimental, in white rat. Turbinate epithelium of squamous type and hyperplastic. (Semenov).

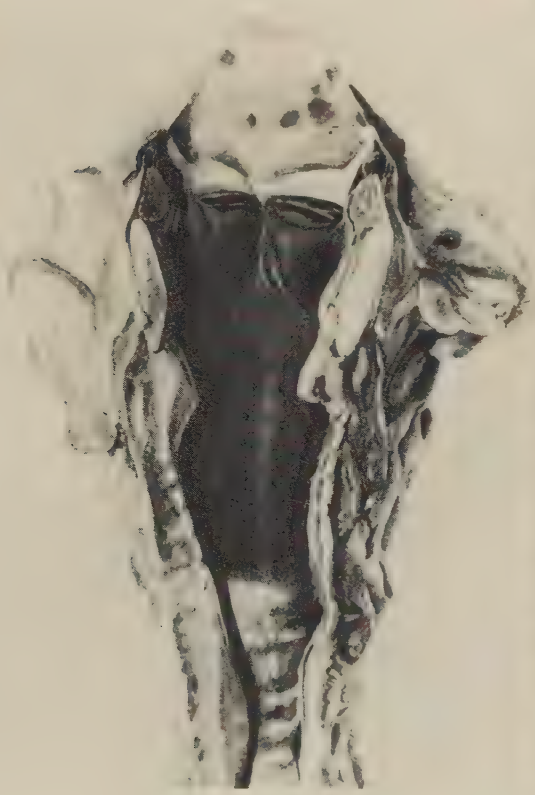
APLASTIC ANEMIA



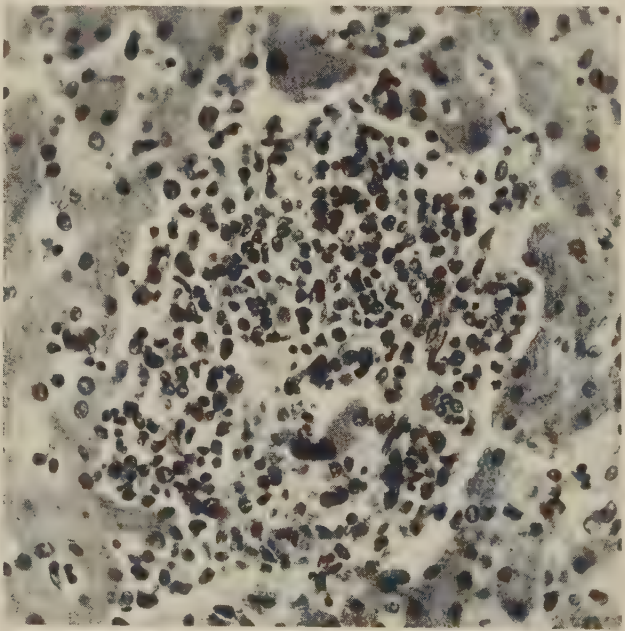
Aplastic anemia, usually caused by ingestion or exposure to toxic substances, including many therapeutic agents. With pronounced leukopenia, as in agranulocytosis, severe necrotizing lesions of the mouth, pharynx and other portions of the upper respiratory tract occur. Ulcerated and hemorrhagic lesions in edematous gingiva are present in this case.



Sclerosis of bone marrow due to extensive bone metastases from a primary carcinoma of the hypopharynx, resulted in an aplastic anemia. The marrow in other instances may be hypoplastic, normoblastic, or hyperplastic.

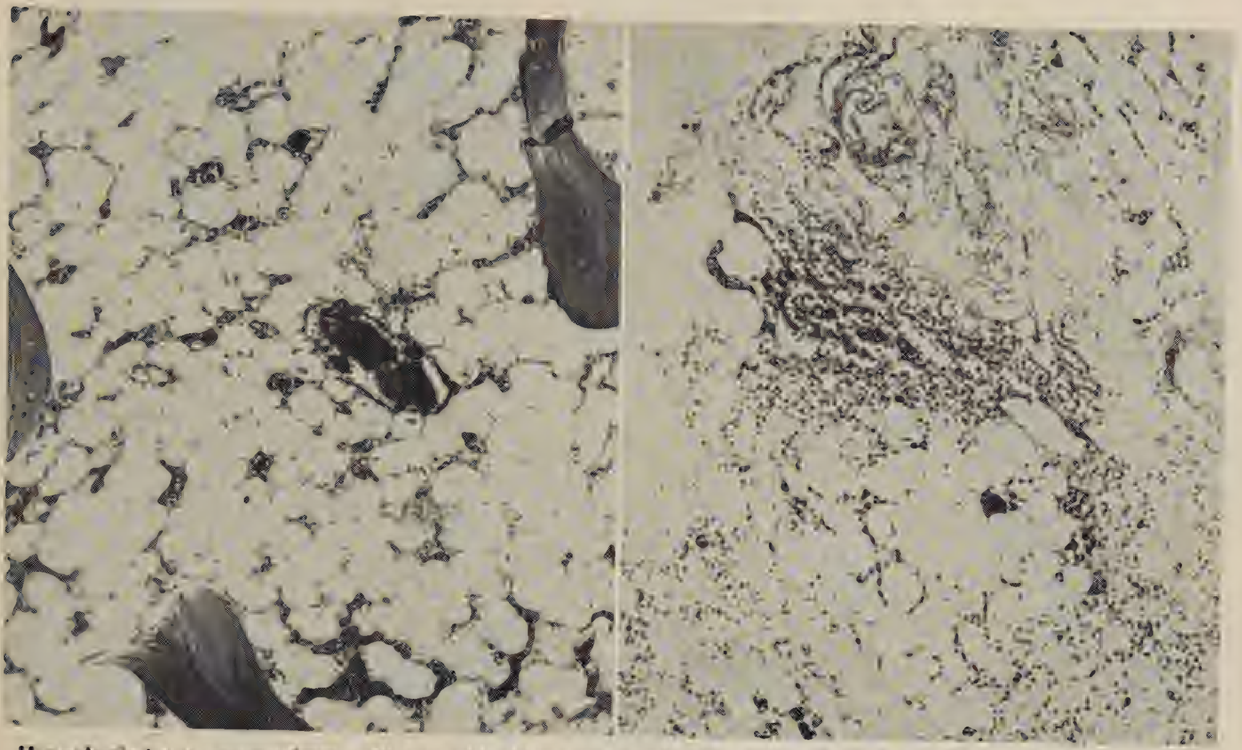


Larynx in aplastic anemia due to sulfanilamide sensitivity with death due to hemorrhagic occlusion of the larynx. Diffusely hemorrhagic laryngeal mucosa, attributable to the thrombocytopenia. Ulcerative lesions of epiglottis and aryepiglottic fold.

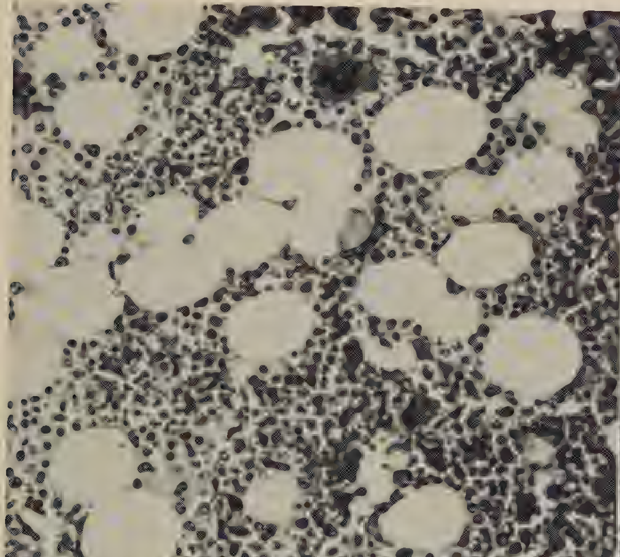


Extramedullary hematopoesis, liver, from case with sclerotic marrow. Note megakaryocyte in center. Cells largely of the leukocytic series, with prominent eosinophilic myelocytes.

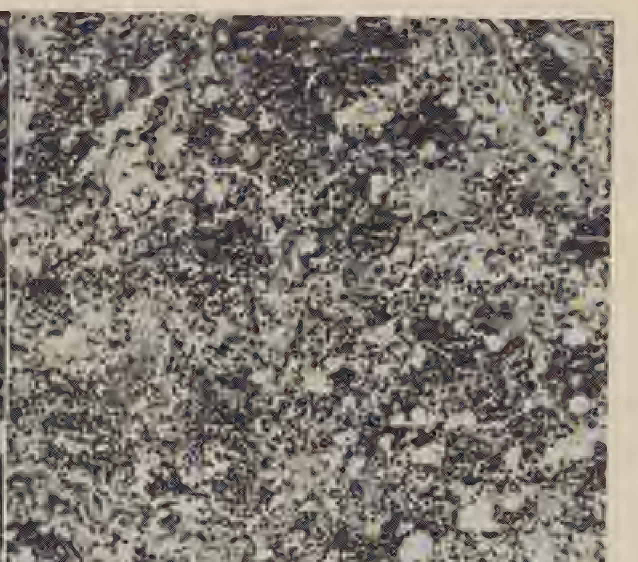
PANCYTOPENIA (CHLOROMYCETIN)



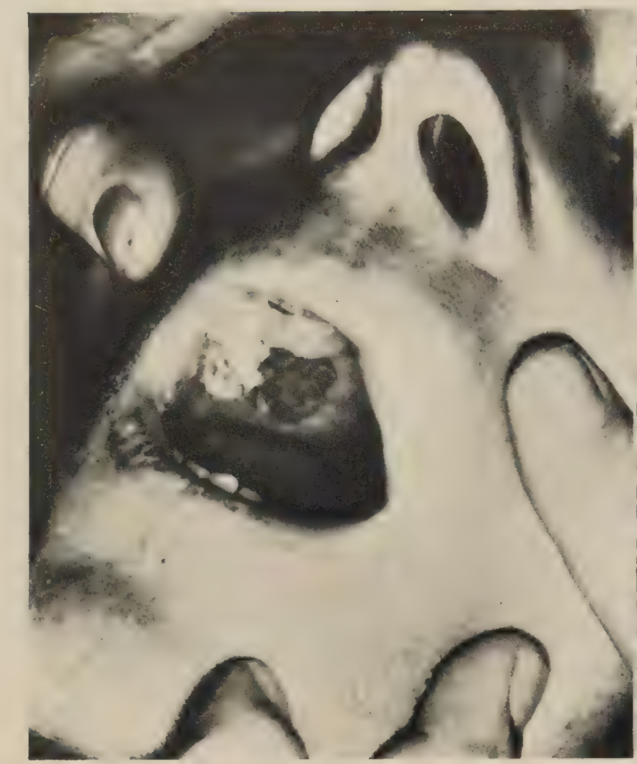
Hypoplastic bone marrow from a 58 year old white woman, who had had prolonged intermittent courses of chloromycetin to control symptoms of bronchiectasis. Empirin, bromoquinine and [one dose of] penicillin were given during a 3 week upper respiratory infection. When hospitalized, she had epistaxis, edema of nasopharynx and ulcerations of uvula and palate. RBC's 3,000,000; WBC's 1,700, all lymphocytes; platelets 24,000. Strikingly hypoplastic bone marrow at autopsy, (left); before death, (right). Both x 90.



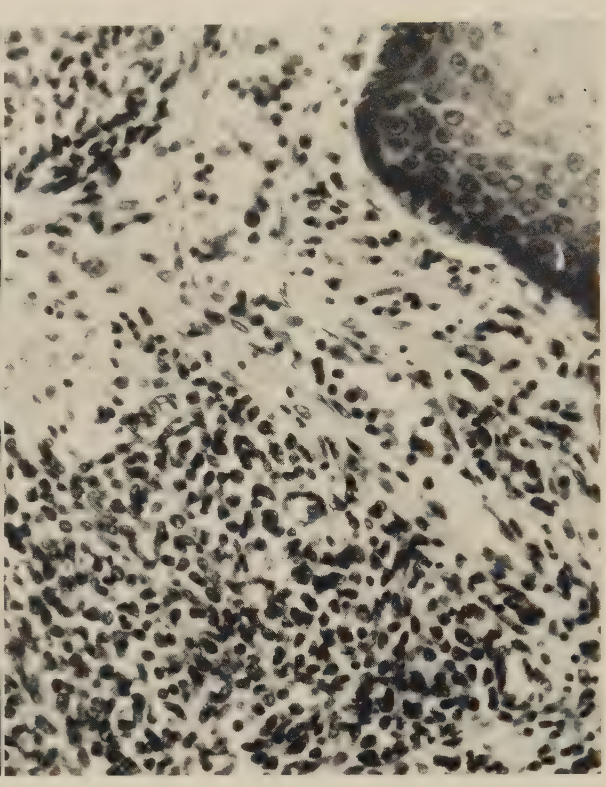
Normal bone marrow, for comparison. x 260.



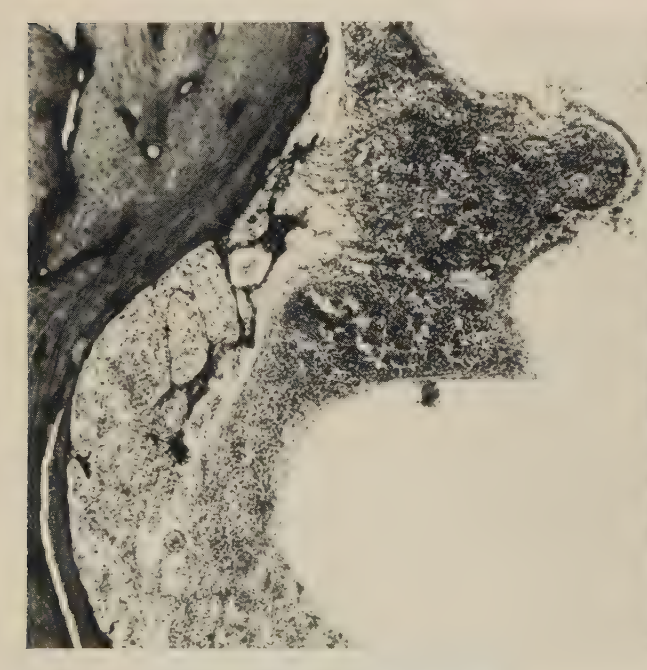
Extensive hemorrhages and edema, lung, x 125 from same case as figures above.



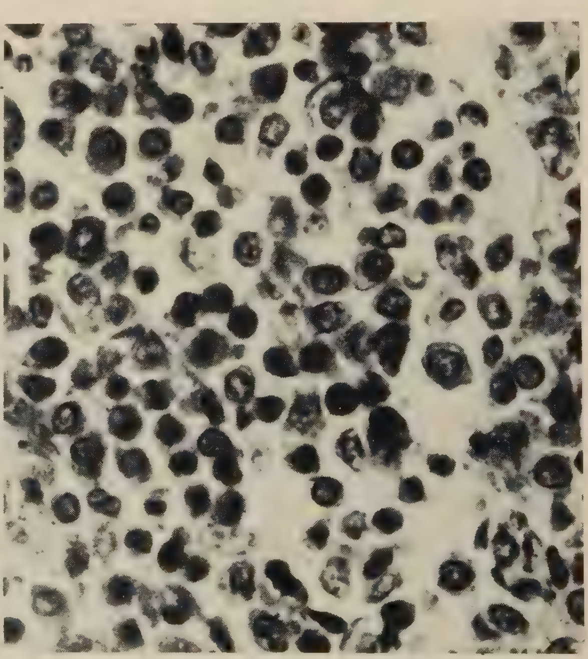
Acute lymphatic leukemia:
Palate, showing puffy mucosa and extensive, freely bleeding ulceration.



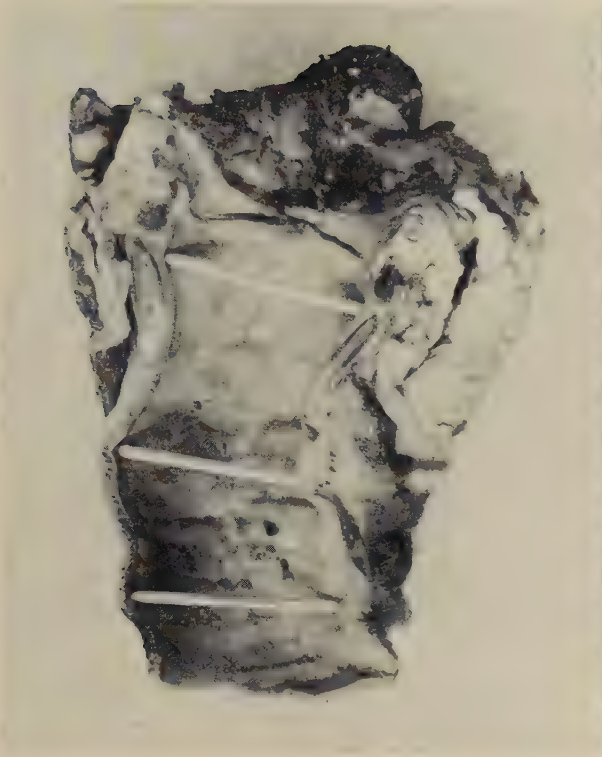
Dense infiltration of gingiva by leukemic cells. Prominent intravascular masses of leukemic cells. x 260.



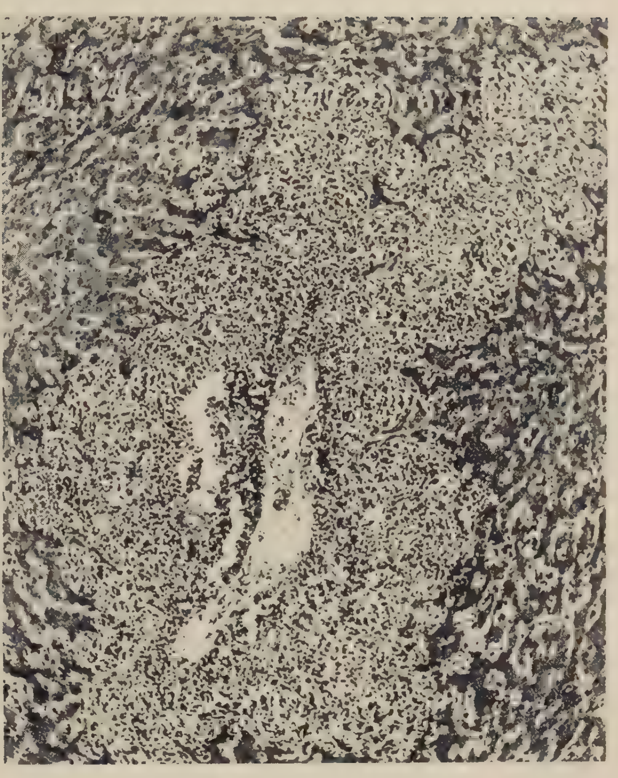
Acute myeologenous leukemia, temporal bone. Labyrinthine mucosa heavily infiltrated. x 48. (S. Guild).



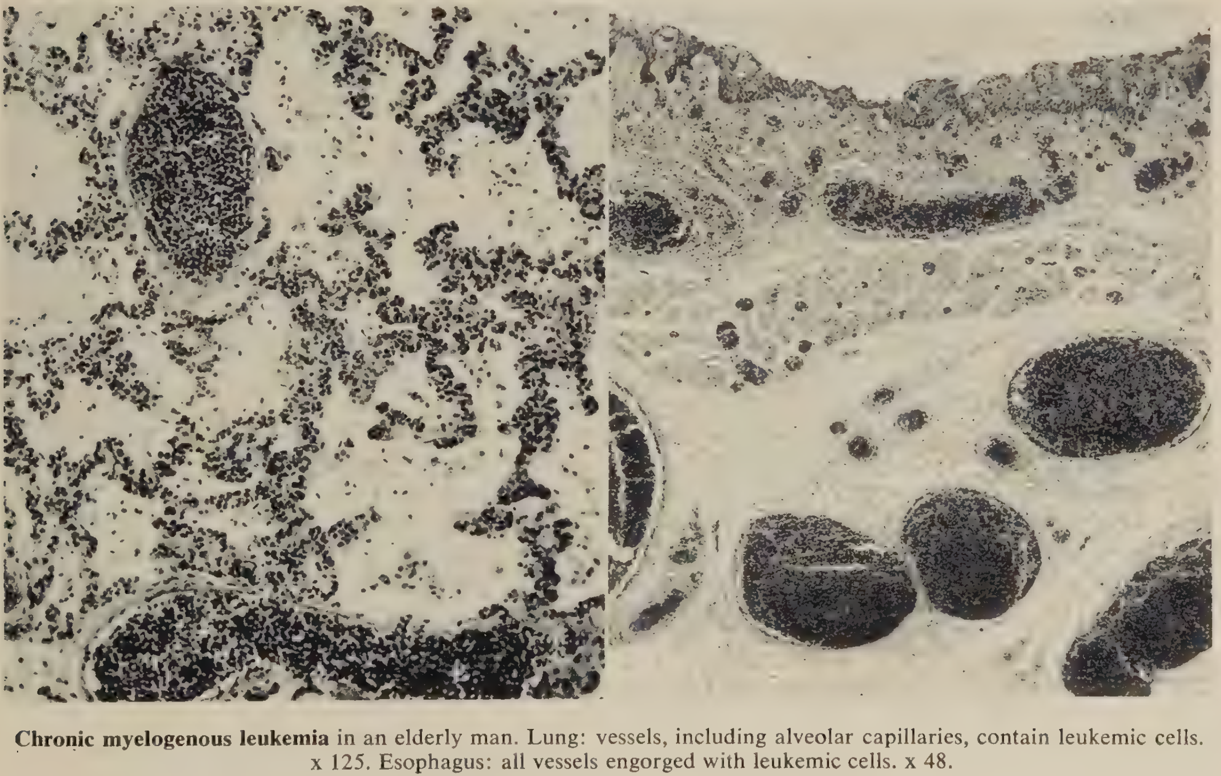
Acute monocytic leukemia, lymph node. Sinusoids contain many large atypical monocytes. x 590.



Monocytic leukemia, resulting in necrosis of the epiglottis and ulcerations in the larynx and trachea.

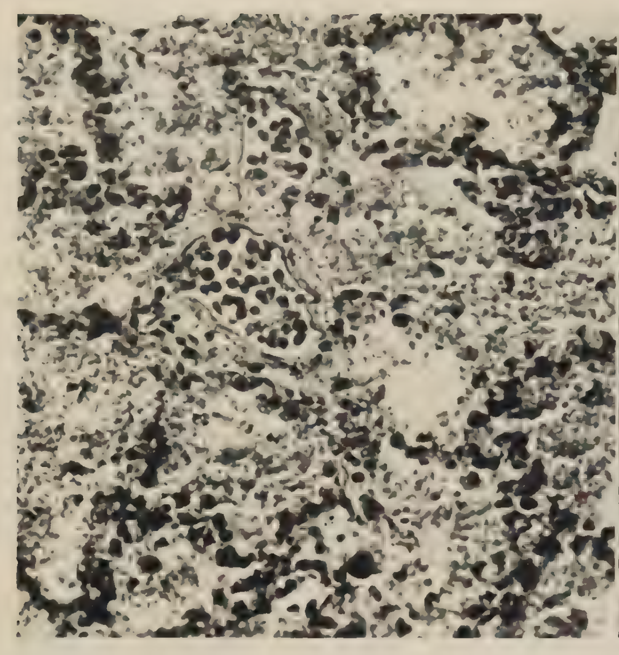


Acute lymphatic leukemia in an 8 year old boy. Extensive periportal infiltration of leukemic cells. x 75.

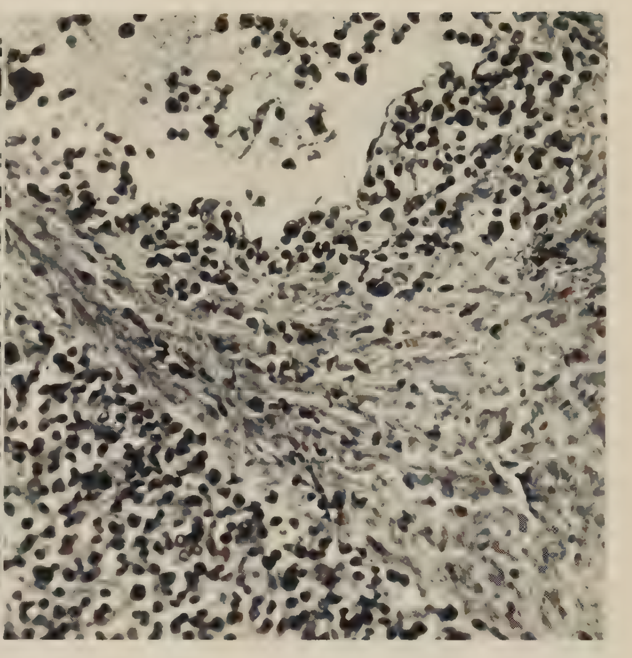


Chronic myelogenous leukemia in an elderly man. Lung: vessels, including alveolar capillaries, contain leukemic cells. x 125. Esophagus: all vessels engorged with leukemic cells. x 48.

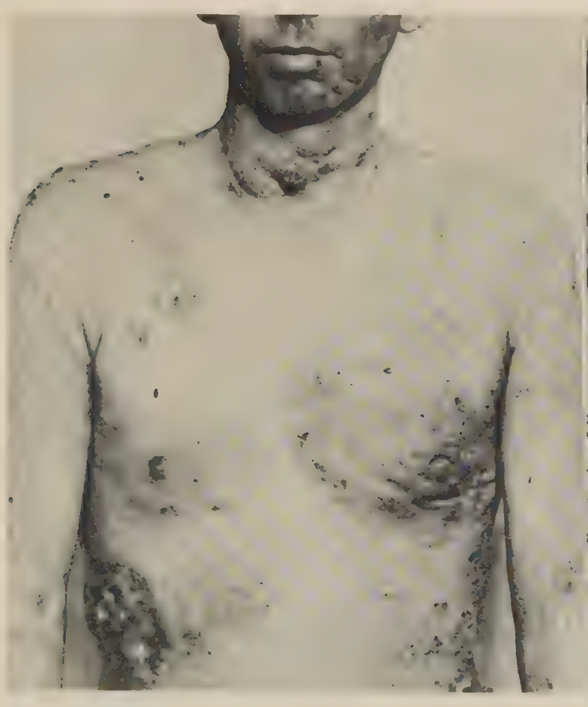
MYCOSIS FUNGOIDES



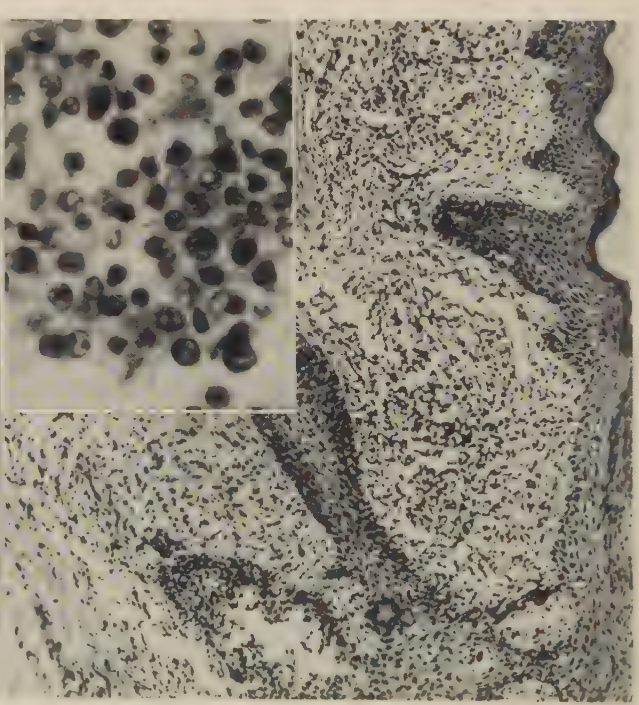
Acute monocytic leukemia. Young male with tonsillitis; massive hemorrhage following tooth extraction. Lung: intra-alveolar hemorrhage. Note leukemic cells in vessels. x 220.



Infectious mononucleosis. Spleen: accumulations of abnormal lymphocytes within vein, in its subintimal zone and in the pulp. x 275.



Mycosis (granuloma) fungoides, stage of tumefaction. A primary cutaneous disease, possibly a primary malignant lymphoma of skin or allied disease. Fatal termination, usually with visceral manifestations, after many years.



Mycosis fungoides. Infiltration of upper dermis with malignant mononuclear cells. Pautrier "abscess" in rete peg at bottom. x 62. Inset: polymorphous cellular infiltrate closely resembling Hodgkin's disease. x 600. The histologic pattern is sometimes that of reticulum cell sarcoma.

CHAPTER 6

LIPID HISTIOCYTOSES AND MISCELLANEOUS DISEASES OF BONE

LIPID HISTIOCYTOSES

Three distinct clinical entities that are manifestations of disturbances in lipid metabolism are the three eponymic diseases, Hand-Schüller-Christian, Gaucher's and Niemann-Pick. They have in common the endothelial cell as a prominent feature. It was formerly assumed that at least the last two were tumors of this cell, but it is recognized now that the basic disturbance is of the metabolism of a lipid and that the endothelial cell is a secondary feature prominent at the sites of localization of the lipid concerned.

A condition associated with Hand-Schüller-Christian disease, and considered by some to be a precursor of it, is eosinophilic granuloma of bone. In addition there are two diseases allied by clinical circumstances and somewhat by histopathology, if not by physiology—amaurotic family idiocy and Hurler's syndrome, or gargoylism.

A brief summary of these diseases and several illustrations are included because they touch upon the field of otolaryngology. In addition to the illustrations in this section, additional ones will be found in the sections on lesions of bones of the skull and face.

Hand-Schüller-Christian disease is characterized by multiple sharply circumscribed defects in the skull and bones of the face in addition to lesions in other parts of the skeleton. Through involvement of the sphenoid, disturbance of pituitary function is possible, resulting in diabetes insipidus and in infantilism. Not infrequently invasion of the orbit results in exophthalmos. When the temporal bone is involved deafness may ensue, and it is usually mistaken for acute or chronic mastoiditis. If at operation, therefore, the picture does not suggest infection, bone should be obtained for histologic examination.

Granulomatous collections of the foamy cells are seen in various organs, but the spotty distribution in the skull is particularly characteristic. The lipid involved in this disease is cholesterol.

Eosinophilic granuloma of bone occurs in children and young adults, and the commonest sites are the ribs and clavicles. When the jaws are affected the teeth lose their normal alignment and become loose. It is more commonly a solitary lesion than is Hand-Schüller-Christian disease and it is possible to eradicate it by surgical removal or irradiation therapy. The lesion in the jaw occasionally simulates an apical abscess, and when the involved tooth is extracted there is a rapid increase in the osteolytic process. Because of the common involvement of the bones of the skull, the roentgenologist must be aware of the disease when he sees multiple areas of rarefaction in roentgenograms that have been made perhaps for other purposes.

Histologically, the material in the rarefied areas shows large numbers of eosinophils, with a small and varying proportion of large mononuclear cells that contain granular material or lipoid vacuoles. There is a background of delicate reticular tissue.

Letterer-Siwe disease, or nonlipid histiocytosis, is generally accepted as allied to Hand-Schüller-Christian disease and eosinophilic granuloma. It is the most serious of the three, in fact it may be the terminal phase of the former. There is a generalized reticuloendotheliosis in which the cells are free of lipid.

Gaucher's disease begins in infancy or early childhood, predominantly in females and those of Jewish ancestry, with splenomegaly that may be discovered accidentally before the more general symptoms of anemia, hemorrhagic tendency and brownish pigmentation of the skin become evident. The disease runs a long course and splenectomy has been successful in prolonging life when the extrasplenic deposits of lipoid histiocytes have not been extensive. When these occur in the bone marrow, anemia results and there are roentgenologic changes in the bones.

The cells in this disease are generally larger than those in the other two diseases, some are binucleated and the vacuolated cytoplasm contains granules and characteristic striations. They are most abundant in the spleen, but are found also in lymph nodes, liver, and bone-marrow, sites of normal reticuloendothelial concentration. The lipid concerned in this disease is kerasin which is not demonstrable by the ordinary lipid stains. Appropriate stains usually reveal iron in the spleen, however.

Niemann-Pick disease roughly resembles Gaucher's, but appears at an earlier age, almost exclusively among Jews, and is invariably fatal in a few years. The lipid-laden cells are more generally distributed than are those in Gaucher's though they are located predominantly in the reticuloendothelial organs—spleen, liver, lymph nodes and bone marrow. The cells are not so large, are more uniform in shape, are vacuolated and react positively to lipid stains. The lipid involved in this disease is sphingomyelin, a phosphatide.

Amaurotic family idiocy, or **Tay-Sachs disease,** is another affliction of the Jewish race. It is apparently a congenital defect that results in characteristic ballooning of the pyramidal cells of brain and spinal cord and the nerve cells in the retina. It manifests itself in early infancy by lack of mental development, by blindness, and by a characteristic cherry-red change in the retinal maculae. It is invariably fatal in a few years.

The nerve cells become enormously swollen and vacuolated, the nuclei and Nissl substance are pushed peripherally, and the neurones become very much thickened. The substance accumulating in the cells includes lecithin, but the entire nature of this process and the pathogenesis of the disease, for that matter, are not known. That it may be an unusual disturbance of lipid metabolism is indicated by the few cases that have been seen in older children of non-Jewish parentage where reticuloendothelial changes like those of Niemann-Pick disease are added to the nerve cell damage.

Gargoylism, Hurler's syndrome, or chondro-osteodystrophy, is a hereditary condition in which, in addition to the disturbances of skeletal growth, there are changes in nerve cells, especially of the anterior horns, and in the reticuloendothelial structures, resembling somewhat those in amaurotic family idiocy and Niemann-Pick disease. The skeletal changes soon become evident in the large head, the frontal ridge, the distorted face, the short neck, kyphosis, and short limbs. Later the spleen and liver become enlarged from the foamy deposits. There is mental retardation, but not the idiocy of the amaurotic disease. Neither is there the blindness of the latter, because optic atrophy and the cherry-red macular change do not occur, but sight is usually impaired because of deposits in the cornea. The vacuoles and eosinophilic granular material can be found in all of the organs, and in this particular gargoylism differs from the lipid dystrophies. The chemistry of the material is not known but it may be related to glycogen.

The children with this syndrome may live for years, not, however, with a very bright future.

MISCELLANEOUS DISEASES OF BONE

As mentioned in the section on vitamin deficiencies, the two classic clinical entities involving bones, scurvy and rickets, are considered here with other diseases involving bone.

Scurvy.—The deficiency in vitamin C (ascorbic acid) interferes with the production and maintenance of intercellular substances in bone, osteomucin and chondromucin. The clinical effects, therefore, are most striking in infants and young children. The effect, however, is also on collagen, dentin, and the supporting substances of the smaller blood vessels. In the active phase a prominent clinical manifestation is the effusion of blood into the tissues, with resulting anemia. These hemorrhages are into muscles, joints, and beneath the periosteum. They are characteristically prominent in the periosteum of the mandible and may also involve the mucous membranes of the mouth. The gums are usually soft and spongy and the teeth become loose. On x-ray examination it is seen that rarefaction of the supporting bony structures is responsible for loosening of the teeth. Another feature of the disorder is developmental deformities in the teeth, particularly irregularities of the occlusal surfaces.

Rickets is caused by deficiency of vitamin D which is an important factor in the metabolism of calcium and phosphorus. Apparently this vitamin acts by influencing the absorption of these important bone elements from the intestinal tract. In vitamin D deficiency the blood content of calcium and phosphorus, particularly the latter, is lowered. Because of the conspicuous effect on the development and contour of bone this deficiency manifests itself strikingly in the very early years of life.

Typical deformities result from the effect on the contour line at the epiphyseal junctions. The rachitic rosary of the costochondral junctions, the funnel breast, or Harrison's groove, from depression of the xiphoid cartilage of the sternum, are two classic features. Rickets may be manifested in the bones of the head by rarefaction and by expansion of the cranium, particularly by bulging of the forehead, bossing, and flattening and thinning of the back of the skull, i.e., cranial tabes. Other deformities of the skeleton result from pressure on the poorly calcified bones.

Restoration of vitamin D balance leads to calcification of the cartilaginous and osteoid tissues, but such deformities as have resulted from the early stages of the disease will persist unless mechanically corrected.

Both the deciduous and permanent teeth show hypoplasia and the enamel is poorly developed. The lymphatic tissue in the pharynx, the tonsils and adenoids is usually hyperplastic. The otolaryngologist may be the first to observe these signs and he should be able to recognize them.

Further consequences of involvement of the skull in the maldevelopment are interference with the normal development of the paranasal sinuses, osteoid exostoses of the skull and into the frontal sinus, and osteoid foci in the temporal bones that may involve the middle ear and bony labyrinths.

The dysplasias of bone are of more than academic interest in our field because they involve so frequently vital portions of the skull, either as part of their systemic distribution or as the sole manifestation of the disease. Nager has studied the involvement of the bony labyrinth in several of the congenital dysplasias. In **chondrodystrophia foetalis** (achondroplasia) he found large and irregular rests of cartilage about irregular areas of ossification; areas of osteosclerosis especially in the cochlear capsule; irregularities in outline of the endosteal capsule; great enlargement of the ossicles by cartilage, with little ossification; and other atypical distributions of cartilage, calcium and ossification. The membranous labyrinth and the lumina, however, were normal.

In **osteogenesis imperfecta,** Nager reported a failure in secondary ossification rather than a disturbance of primary chondral formation. This leads to severe changes in both the periosteal and enchondral layers, deformities of the cochlea, and the absence of normal lamellar bone. These patients have failing hearing and otosclerosis is sometimes found.

Osteitis fibrosa cystica, von Recklinghausen's disease of bone, is due to increased production of parathyroid hormone (parathormone) either as a result of an adenoma or of diffuse hyperplasia of the parathyroid glands. This causes, as in vitamin D deficiency, a disturbance of calcium and phosphorus metabolism, resulting in resorptive changes in bone, manifested as bone cysts or as generalized osteoporosis. While the long bones are most commonly involved, the mandible, maxilla and temporal bones are occasionally included in the process. Roentgenograms reveal circumscribed areas of bone destruction.

Microscopically, these lesions show a loss of normal bony trabeculae and their replacement, as well as that of the marrow spaces, by fibrous tissue and osteoclastic giant cells. In the earlier stages this fibrous tissue is perivascular in distribution, but with the peripheral advance of the process vascularity decreases and the collagen content increases.

In the more advanced lesions gross cysts develop. The process is expansile and pathologic fracture is a not uncommon result and may be the initial indication of the disorder. The giant-cell content at times makes the differentiation from endosteal giant-cell tumor difficult. Skeletal x-ray survey and determination of the blood calcium and phosphorus are essential diagnostic procedures. The blood calcium is increased and the phosphorus decreased in the hyperparathyroid state.

Solitary bone cysts may be the end result of hemorrhage or of traumatic destruction of central bone. On x-ray and histologic examination these cysts may be indistinguishable from those of the von Recklinghausen syndrome.

Osteitis deformans, Paget's disease of bone, usually a systemic bone disease, is occasionally limited to one or more bones of the skull and face. The real cause of the condition is not known, although it seems to be on a hormonal or metabolic basis. It is more common in women in later life. As in acromegaly, the mandible may be the first part of the skeleton involved. This is evidenced by the loosening of the teeth because of the excessive production of cementum on the roots. Difficulty in chewing and swallowing are early symptoms, or the first manifestation may be general enlargement of the cranium. When the temporal bones are involved, tinnitis aurium and nerve deafness are common early symptoms. The blood usually shows an increase in alkaline phosphatase and in calcium but a decrease in phosphorus. On x-ray examination excess porosity of the involved bone and later obliteration of normal marrow cavities are seen.

The occasional occurrence of bone sarcoma as a complication of Paget's disease must be borne in mind.

Grossly, the affected bones are quite characteristic. Those of the calvarium are greatly thickened but soft and diffusely cancellous and can be readily cut with a knife. The pronounced vascularity is evident in the pinkish color of the bone.

Microscopically, the characteristic mosaic pattern in the osseous tissue can be seen best in tissues that have not been too thoroughly decalcified during preparation of the slides. This peculiar architecture of wavy cement lines between the old and new tissues is the result of the very active osteoclasis which produces deep and irregular lacunae and of the simultaneous deposition of layers of osteoid tissue which becomes calcified. The normal fatty marrow is generally replaced by vascular connective tissue and areas of dense bone.

The localized form of osteitis deformans involves most commonly one of the skull bones or the mandible. The general disease may begin as a local manifestation; it may even be limited to an area of osteosclerosis in a jaw.

An example of the disease limited to the sphenoid is included in the illustrations for this section and one involving the temporal bone will be seen in the section where that structure is discussed. The first case was that of a 31-year-old colored man, who, for over a year, had suffered from neurologic symptoms of increasing severity caused by pressure on the pons, producing severe internal hydrocephalus. He died suddenly from respiratory paralysis. Roentgenograms had shown complete obliteration of the sphenoidal sinus with great reduction in the size of the sella. At autopsy, the cribriform plates of the ethmoid and the body and lesser wings of the sphenoid including the sella were greatly thickened, cancellous throughout, and soft in consistency. This form is called osteoporosis circumscripti cranii.

Another case illustrating the more usual picture was that of a 62-year-old colored woman who first complained of loosening and extrusion of the teeth in the mandible. She felt that her mouth had been growing smaller for 10 years. There was no pain or discomfort. The mandible was extremely large with the crowns of the lower teeth pointing labially. Blood calcium and alkaline phosphatase were increased and blood phosphorus decreased. The x-rays showed involvement of the skull as well as the mandible.

Tamari has recently reviewed the subject of osteitis deformans as it involves the temporal bone. Clinically, conductive deafness may occur in the early stages, later becoming of mixed type and finally total. The pathologic changes are usually bilateral and stand out clearly in contrast to the easily recognized structure of the normal bony capsule. The endosteal inner layer being particularly poor in vascular marrow is least changed, the middle enchondral layer is also somewhat resistant, while the outer periosteal bone, well supplied with vascular marrow spaces, is earliest and most characteristically transformed into typically mosaic new bone. This new bone finally deforms the inner layers in hump-like formations that eventually influence the functions of the membranous labyrinth, and are manifested clinically by tinnitis.

Osteomalacia is the adult counterpart of rickets. It is seen most commonly in women who have had several pregnancies and in very old people. In these patients the condition is chiefly the result of the withdrawal of calcium from the bones rather than deficiency in the primary deposit, thus it is not manifested prominently in the bones of the skull. When the temporal bones are involved, however, the results are particularly striking because of the new bone growth in the labyrinthine capsule which is normally quiescent throughout most of life.

Microscopically, the bones in rickets and osteomalacia show an osteoid matrix surrounding the primary calcified bone lamellae and a varying amount of fibrosis of the marrow tissue. In rickets there are additional prominent disturbances of the growth line, particularly manifested by great irregularity in the epiphyseal cartilage plates.

Acromegaly (gigantism) is a disease of adult life, the result of hyperpituitarism whereby production of growth hormones is increased. X-ray examination of the skull will reveal enlargement of the sella turcica. Clinically, thickening and enlargement of the soft parts of the face and tongue are initial manifestations, and through endochondral ossification at the condyle, great enlargement of the mandible occurs early to produce the prognathous aspect. This involvement of the bone and soft parts leads to the clinical picture of leontiasis facei.

Fibrous dysplasia of bone (Lichtenstein and Jaffe) is another syndrome which in its fully developed state (Albright's syndrome) includes multiple bone lesions (polyostotic fibrous dysplasia), skin lesions, particularly café au lait spots similar to those seen in multiple neurofibromatosis, and evidences of endocrine dysfunction, including precocious puberty in females (Albright's syndrome).

In a number of cases, however, the condition is limited to the bone lesions, and in another group there is only one bone lesion (monostotic fibrous dysplasia). It is this form that is most commonly found in the bones of the jaws. It seems unlikely that the monostotic and polyostotic forms are on the same etiologic basis, although they cannot be differentiated histologically. It is possible that the monostotic lesion is on a traumatic basis as is the solitary bone cyst. The solitary lesion has been identified by some as ossifying fibroma, by others as fibrous osteoma, and the present tendency is to consider it more likely a neoplastic process than a dysplasia. It is argued that the osteoid spherules seen in the solitary lesions of the maxilla are not so common in the fibrous-dysplasia lesions in other bones. The trabecular, fish-hook type of osteoid is characteristic of dysplasia. It is true, also, that the lesions in the jaws are clinically more aggressive than those in other bones; they usually are more difficult to eradicate and may involve the maxillary sinus and expand into the nose, orbit and sphenoid, a common occurrence with neoplasms in this site. Tumors and cysts of the mandible and maxilla are covered in the division on the nose and paranasal sinuses.

In a group of 67 cases of the monostotic disease in the files of the Armed Forces Institute of Pathology studied by Schlumberger, none showed skin pigmentation, congenital anomalies, or endocrine disturbance. Seven lesions were in the maxilla, two in the mandible, five in the calvarium, and one in the mastoid process of the temporal bone. This involvement of the bones of the skull and face may lead to gross deformities. As a matter of fact, it has been suggested that fibrous dysplasia is one of the causes of leontiasis. The lesions in Schlumberger's series produced exophthalmos, facial asymmetry and swelling behind the ear, depending on the site of the lesion.

There is no significant alteration in blood chemistry, an important differentiation from osteitis fibrosa cystica with which it may be roentgenologically and pathologically confused. In the monostotic form the prognosis is good. When weight-bearing bones are involved there may be pathologic fractures, but complete excision of the lesion has proved effective in halting the process.

It is seldom possible by x-ray alone to differentiate the lesion from any of the other circumscribed osteolytic processes, except for the lesion in the calvarium which tends to break through the outer cortex, as shown in the following figures.

Pathologically, an intact but thin layer of cortical bone usually covers the involved area in which normal structures are completely replaced by firm, yellowish-white tissue, sometimes containing small cysts. The material is usually gritty because of the many very small spicules of bone.

The histologic picture is varied. There is a general background of connective tissue which may be highly vascularized in the periphery. Areas of numerous giant cells of the osteoclastic type may be a forerunner of cyst formation in the fibrous stroma by destruction of newly formed bone. The picture is further characterized by areas of osteoid and by groups of lipid-containing histiocytes. Cartilage is generally not found unless there has been a fracture of the bone. The connective tissue element at times is so cellular as to present a whorling which Schlumberger considers characteristic of the condition. This feature has led to an erroneous interpretation of sarcoma.

A rare familial congenital osteodystrophy of incidental importance because it involves the jaws and skull is **cleidocranial dystrophy.** There is retardation in the closure of the fontanels, protrusion of the mandible, hypoplasia of one or more of the bones of the skull, and hypoplasia or absence of one or both clavicles.

Additional discussion and illustrations of the osteodystrophies will be found in the section on the temporal bone.

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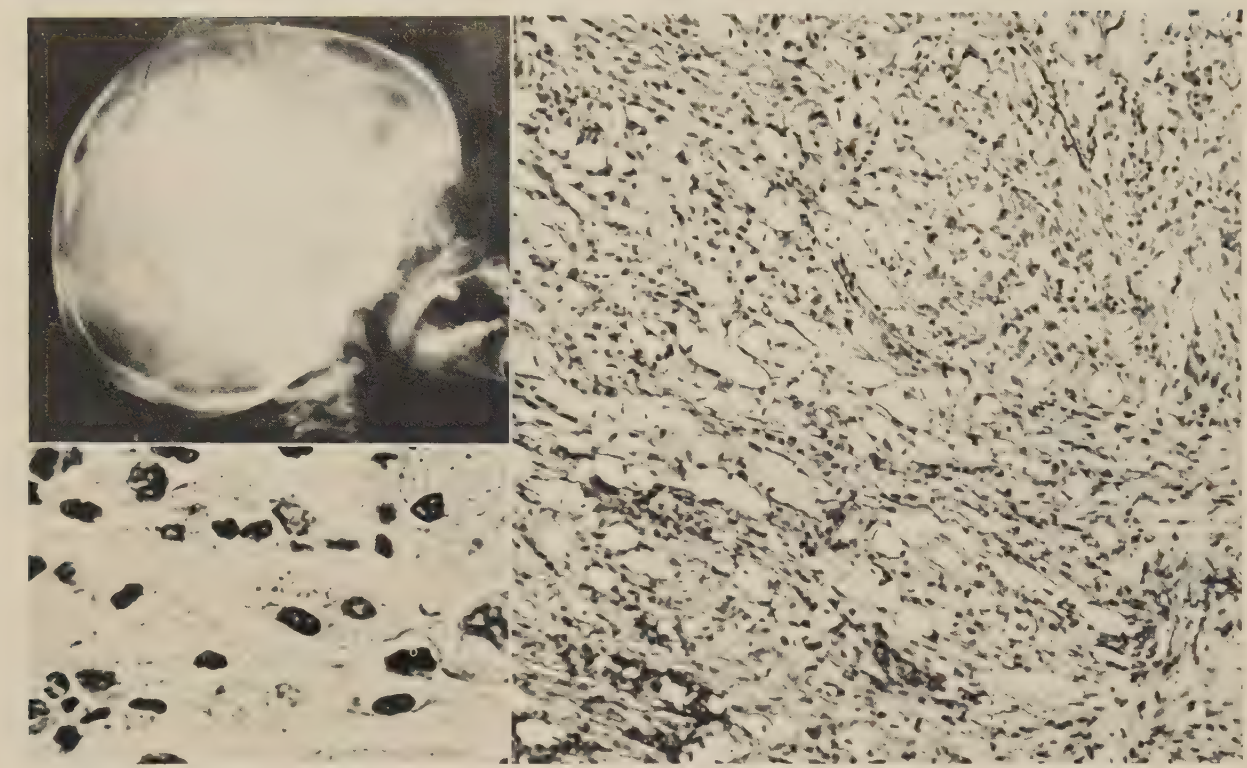
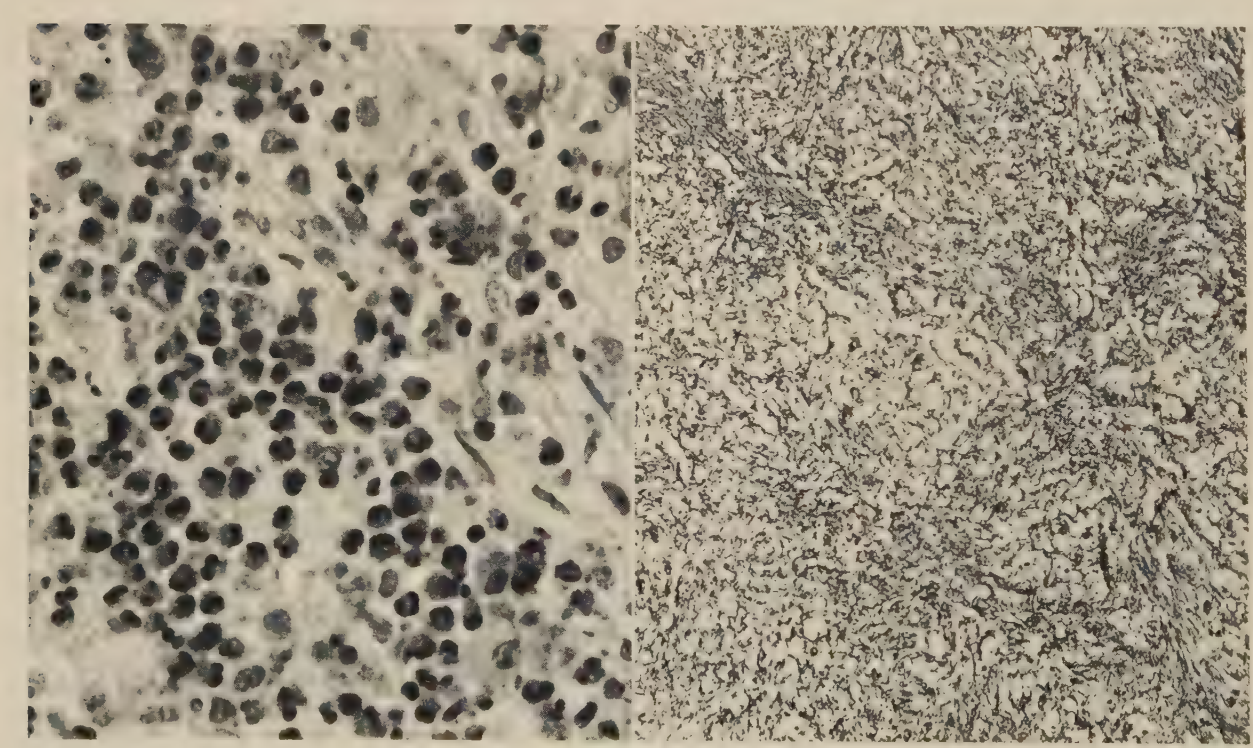
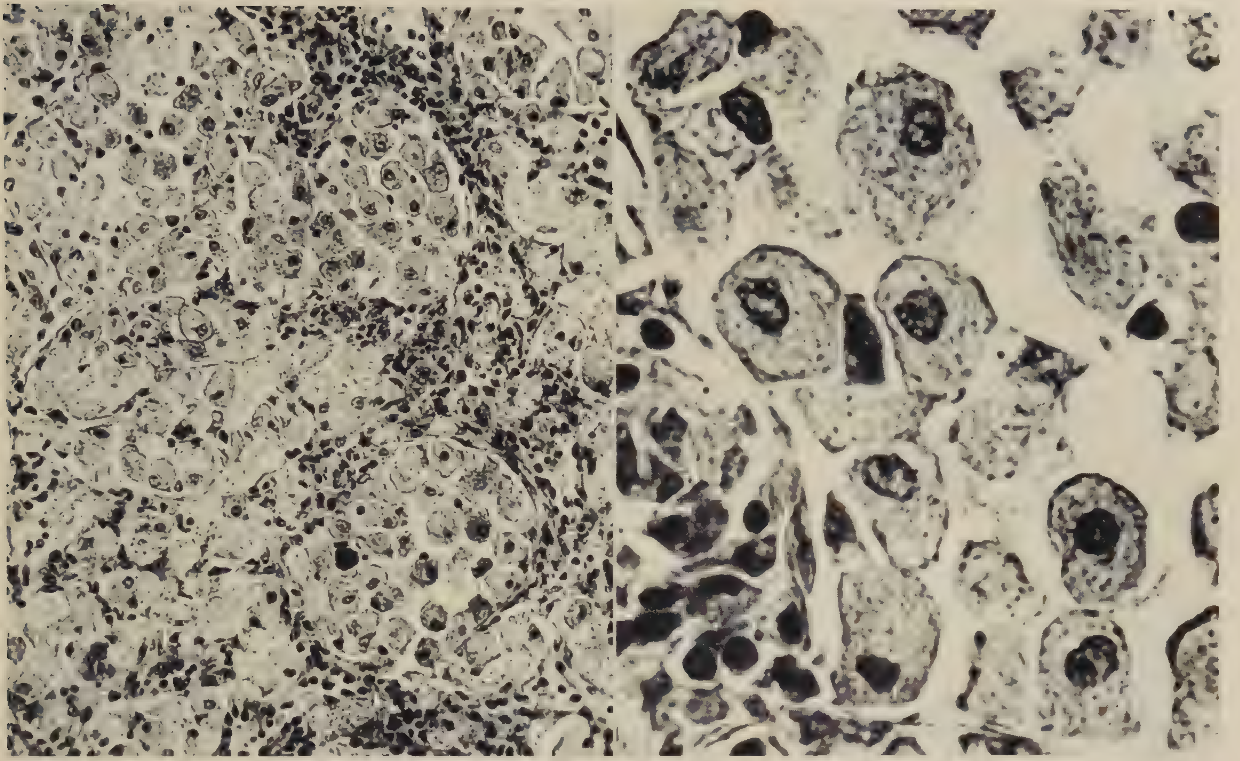


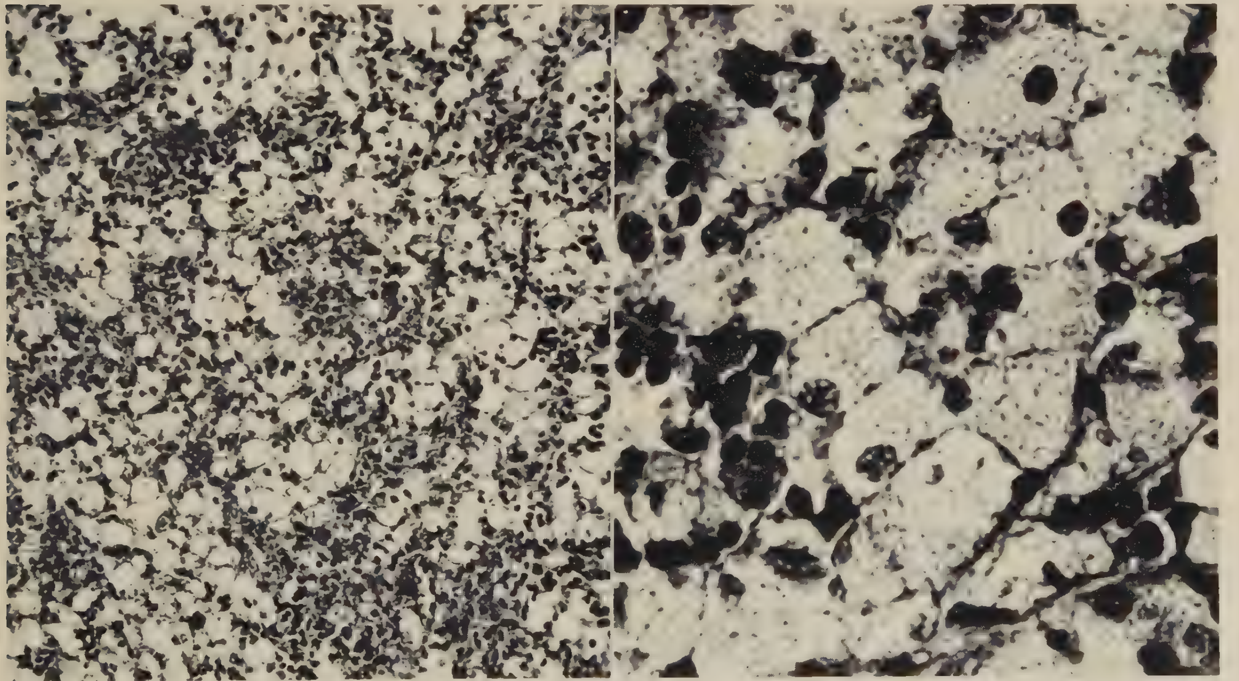
Hand-Schüller-Christian disease: A. X-ray of skull revealing the typical moth-eaten condition of the calvarium. B. Entire thickness of the bone replaced by cellular fibrous tissue containing many cholesterol-laden histiocytes. x 205. C. Foamy character of cells is seen at left. x 700.



Eosinophilic granuloma of bone: D. Very dark cells in mass are eosinophils, both mononuclear and polynuclear. There are several foam cells. x 550. E. Other portions of the lesion may be dense fibrous tissue, with foam cells, but few if any eosinophils. x 90.

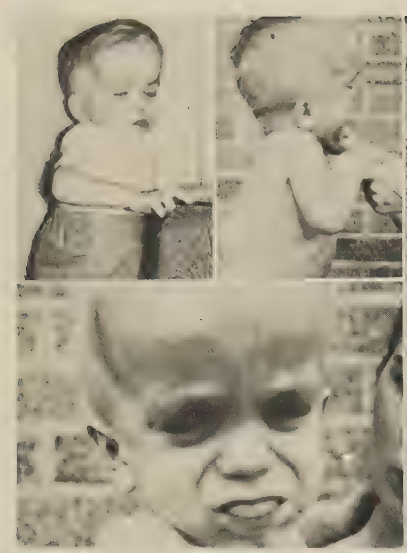


Gaucher's disease. Kerasin lipidosis involving spleen, liver, bone marrow and lymph nodes. *Left:* architecture of enormously enlarged spleen obscured by pale reticuloendothelial cells laden with the cerebroside, **kerasin.** x 185. *Right:* the "Gaucher cells" are large, ovoid or spherical, with relatively small nuclei with distinct nucleoli. The cytoplasm is characteristically striated and fibrillar ("cat-scratch markings") or granular. x 900.

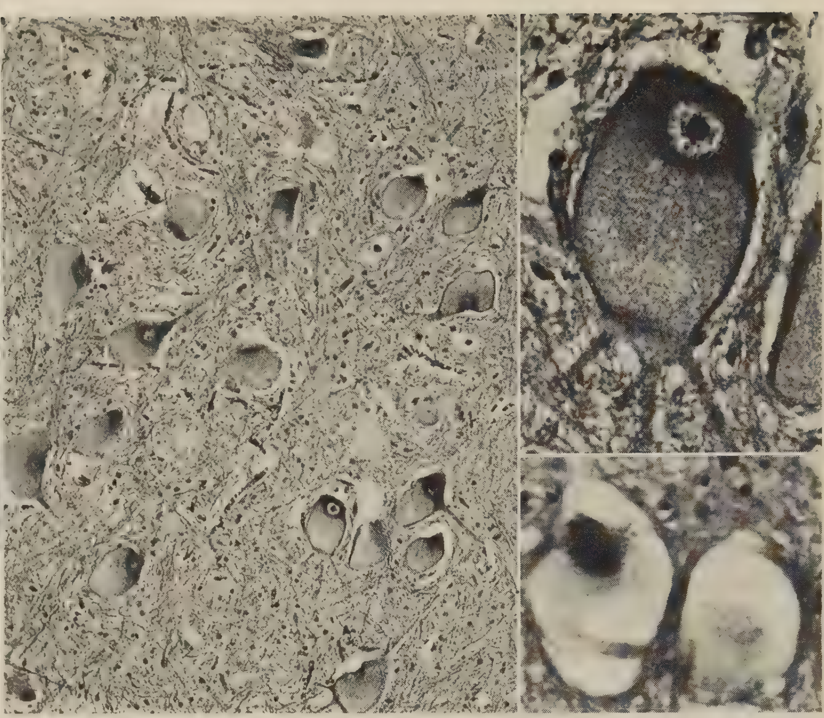


Niemann-Pick disease: Rapidly progressive disease of infants, with more widely distributed lesions and fatal termination in less than 2 years. *Left:* spleen with foamy vacuolated reticuloendothelial cells which contain **sphingomyelin.** x 185. *Right:* cells with clear cytoplasm containing small round vacuoles. This feature and specific staining characteristics enable histologic differentiation from cells of Gaucher's disease. x 800.

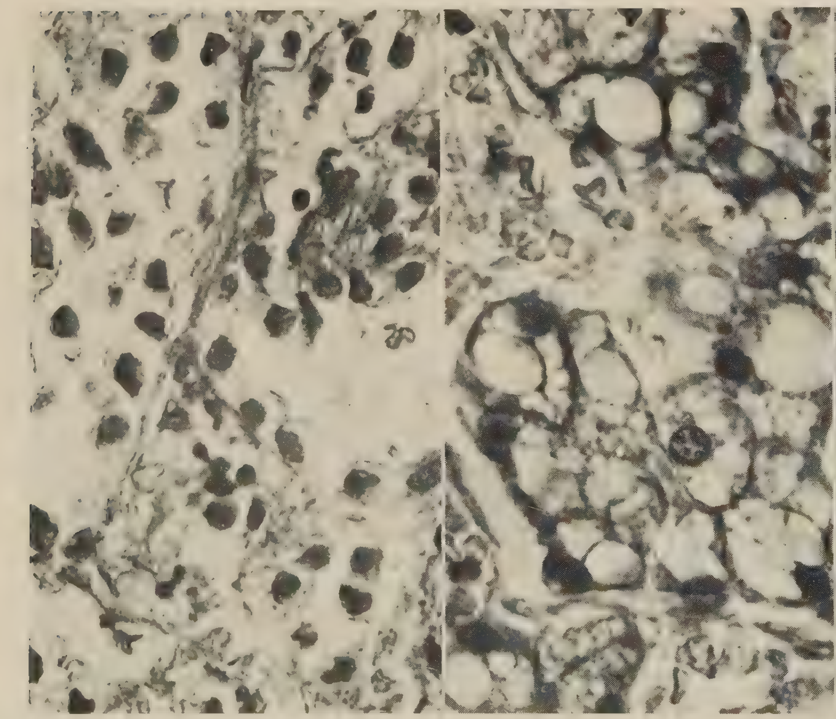
GARGOYLISM



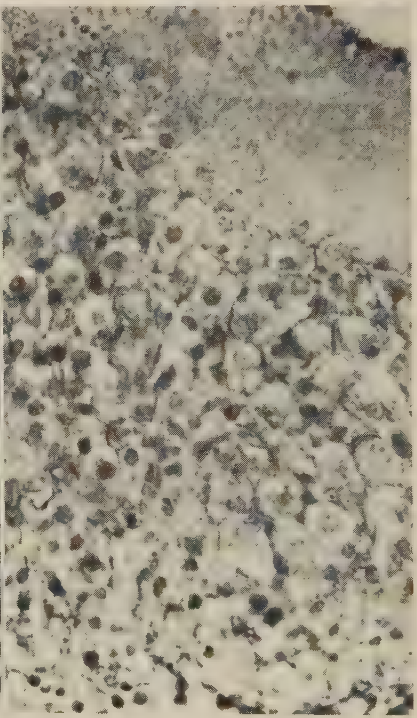
Gargoylism (Hurler's Syndrome): The clinical pictures show dwarfism, dorsolumbar kyphosis, short neck, large skull with frontal bosses, coarse features and protruding tongue. (Arthur Morris, Washington, D. C.)



A. Grotesque ganglion cells in spinal cord in gargoylism. x 165. Grotesque cell (B, x 900) compared with cells from retina in amaurotic family idiocy (C, x 300).

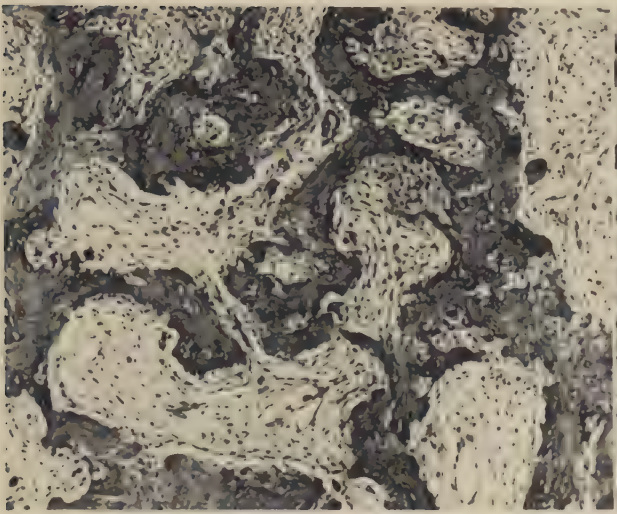


D and E. **Gargoylism.** Dystrophic changes in spleen (D), showing large atypical endothelial cells (x 900), and in liver (E), occupied by large foamy cells (x 900).

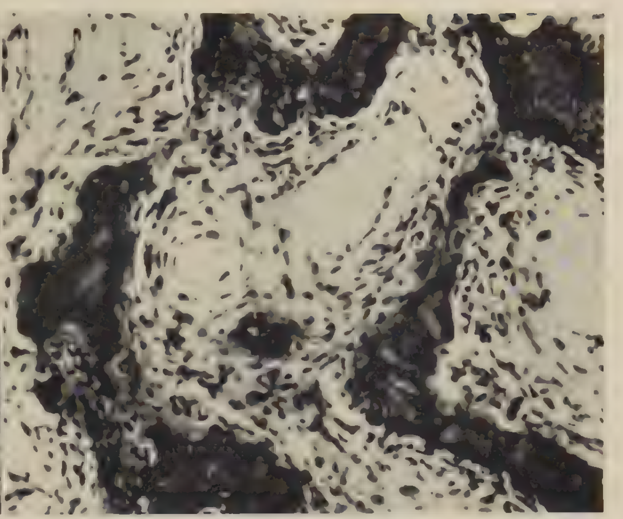


Amaurotic family idiocy. Collection of the lipid-laden ganglion cells in retina. x 475.

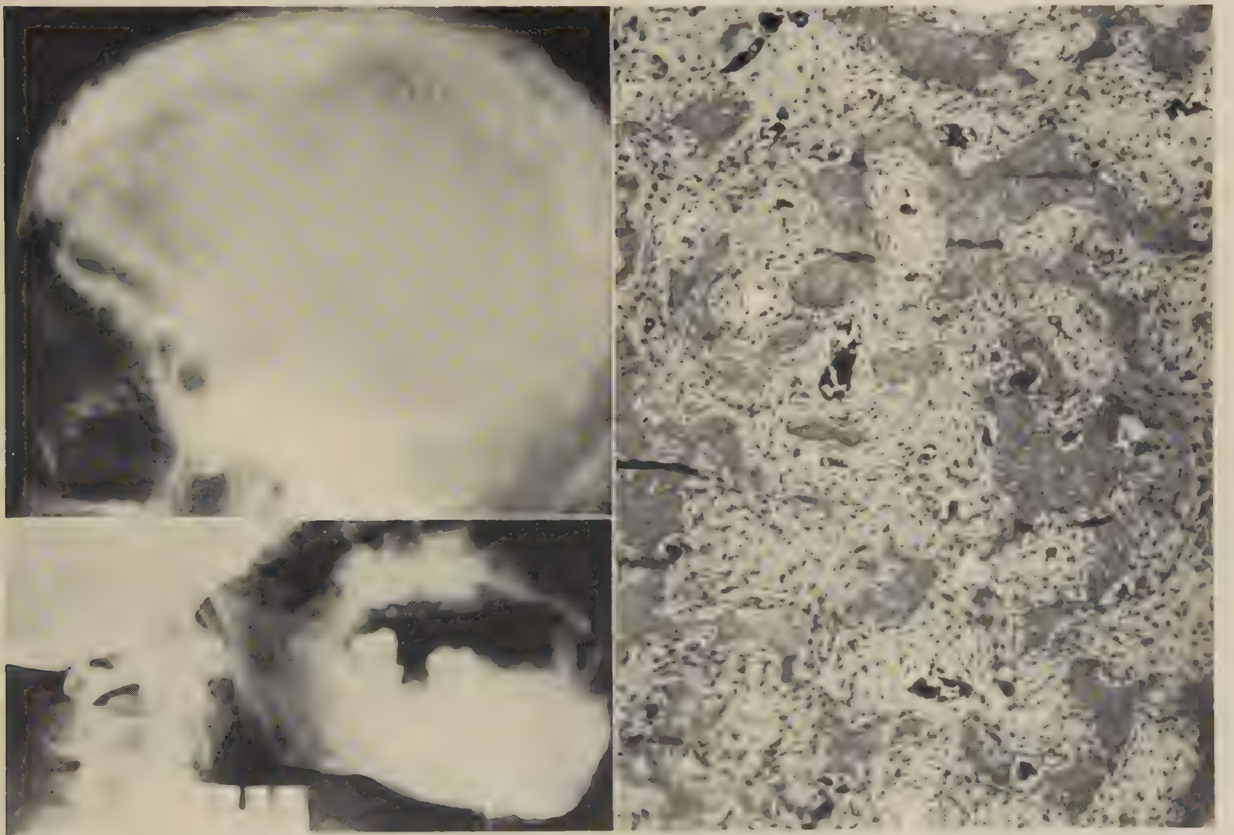
POLYOSTOTIC FIBROUS DYSPLASIA
OSTEITIS FIBROSA CYSTICA-OSTEITIS DERFORMANS



Polyostotic fibrous dysplasia. 23 year old male with multiple skull and skeletal lesions, asymmetrical face and skull. Unusually thick nasal septum resected because it obstructed airway. Extremely irregular bone trabeculae, many spiral and curved, in moderately cellular fibrous tissue. x 145.



Osteitis fibrosa cystica in case of primary hyperparathyroidism with multiple osteoporotic lesions and elevated serum calcium. Active osteoclastic resorption of bone, with replacement by fibrous tissue. Microscopic cysts at top. x 330.



Osteitis deformans (Paget's disease). X-rays: abnormally large and thickened calvarium with irregular "fuzzy" surface, due to replacement of normal smooth compact cortical bone by extensive deposition of new trabeculated bone. Dense enlarged mandible and alveolar processes of maxilla show unusual involvement. Other facial bones spared. Right, irregular "mosaic" pattern of lamellated bone produced by simultaneous resorption and osteogenesis. Note osteoclasts in deeply notched margins. Prolonged decalcification of the specimen has made cement lines inconspicuous.

CHAPTER 7

THE EFFECTS OF IONIZING RADIATIONS

Tragic experiences through the years with the late results of irradiation have dampened the early enthusiasm for the use of x-rays and radium for the treatment of benign conditions. Disfiguring atrophy and scarring of the face developing years after a supposedly innocuous dose of x-rays for the treatment of acne or birth marks; permanent epilation resulting from the injudicious use of x-rays in the treatment of fungus diseases of the scalp, and sarcomas and malignant epidermal tumors arising on the basis of a chronic radiodermatitis years after single or multiple exposures to minimal doses of ionizing radiations, all have inspired a healthy respect for these powerful physical agents. The good they can do is immediate, but "the evil they do lives after them" and is generally irreversible. Under no circumstances, therefore, is exposure to any form or dosage of ionizing radiation to be taken lightly, from that necessary in the treatment of malignant lesions down to that incident to the handling of the nasopharyngeal radium applicator used by so many otolaryngologists.

There is individual variation in the degree of sensitivity to irradiation just as there is to sunlight. It is not within our province to go into the details of this pertinent and fascinating subject, but only to indicate the obvious pathologic effects of over-exposure and to review the morphologic changes that result from therapeutic irradiation, with special reference to the pharyngeal lymphatic tissue.

As a rule, the more highly differentiated cells are more resistant to irradiation, and sensitivity increases as the cells come closer to the undifferentiated embryonal type. In addition, certain specific tissues are more sensitive than others. Good examples of this are the lymphatic tissue and the vascular neoplasms. In a given type of cell those undergoing mitosis are more sensitive than the mature quiescent cells. This is one of the reasons that actively growing tumors respond more favorably to irradiation than do slowly growing, well differentiated ones.

To ordinary therapeutic doses there is an early evanescent vascular reaction in the exposed skin. In addition there may be more delayed and serious reactions of two types, one, radiodermatitis, the other, keratosis. Both may be present.

Radiodermatitis is characterized by a mixture of hyperplasia and atrophy of epithelium, dilatation of the superficial blood vessels, fibrosis of the dermis, and obliterative changes in the larger vessels in the deep dermis and in the subcutaneous tissues. As a usual result of the vascular damage, areas of necrosis extend from the surface deep into the skin. The epithelium shows areas of vacuolation and some scaling. The connective tissue cells undergo a characteristic change. Some become large with considerable cytoplasm and they may be multipolar.

Exposure of the buccal mucosa to irradiation is indicated by the development of a yellowish membrane.

Irradiation keratosis is a focal exaggeration of the hyperplasia of the epithelium and is practically always associated with radiation dermatitis. It is of particular significance, for in addition to hyperplasia there is dyskeratosis of the type seen in senile precancerous lesions of the skin. Frank carcinoma develops in these keratoses.

The great, though delayed, danger from repeated but otherwise innocuous exposures to radiation is the accumulation of radioactive particles in the bone marrow. This was brought to attention some years ago by the experience of the painters of luminous watch dials. After years of exposure to the accumulating particles of radium, blood dyscrasias, extensive necrosis of bones, especially of the mandible, and, in a number of instances, bone sarcoma developed. The discouraging feature is that years may pass before the effects are evident and then the changes are irreversible and progressive.

Histologically, non-inflammatory necrosis of bone is evidenced by the loss of bone corpuscles and fibrous replacement of fatty marrow. There is active osteoclasis but very little replacement of bone because the osteoblasts of the periosteum are largely destroyed, and sequestration does not occur.

Effects of Atomic Explosion.—The material collected by the joint Army and Navy Commission from the Hiroshima and Nagasaki victims of the atomic bomb shows the terrific effect of generalized exposure to an enormous dosage of radiation. While the majority of the casualties were from blast, fire and secondary missiles, some of the victims died directly from radiation effects. Those of the exposed who survived could be divided into three rather well defined clinical groups which represented exposures of varying intensities. In the first, because of almost complete destruction of the hematopoietic system, a hemorrhagic state developed in a few days, and in a week or ten days death resulted from hemorrhages and secondary infections especially prominent about the mouth, nose and eyes. The lymphatic tissue of the nasopharynx was practically eliminated, and in spite of severe infection polymorphonuclear cells were sparse or absent in any exudate. There were profound changes in the epithelium of the mucosae: destruction of much of it, marked hydrops and degenerative changes, and bizarre forms among the cells still alive.

The second group obviously had marked suppression of the hematopoietic system, profound changes in the gastrointestinal tract, and epilation. In the course of weeks or months, however, many recovered, but with sufficiently lowered resistance to fall victim to infections, particularly tuberculosis.

The third group went through a mild acute phase of gastrointestinal symptoms, a mild hemorrhagic episode, and some epilation, but the acute changes were entirely reversible. Remote effects are still to be demonstrated by future observation, and the possible mutation effects due to gene translocations will not be evident for another generation or more.

X-rays in Treatment.—Looking on the brighter side, much good can be accomplished by the skillful use of x-rays and radium. Intensive x-ray therapy is the only means of controlling the surgically inaccessible nasopharyngeal and the inoperable hypopharyngeal carcinomas. The dermatologist is generally successful in eradicating the superficial basal cell carcinoma by radium or x-ray. Of course, there is the occasional tragedy when he has depended on his clinical rather than histologic diagnosis and has irritated a malignant mole into generalized metastasis.

The use of radium in the nasopharynx during the last war was a great help in reducing aerotitis among aviators. The susceptibility of lymphatic tissue to irradiation made it possible to reduce excess lymphatic tissue that interfered with the proper functioning of the auditory tube. The exposure of the region of the torus tubarius to minimal doses of irradiation proved to be an effective way of controlling the incapacitating aerotitis resulting from obstructing amounts of lymphatic tissue in the nasopharynx. Fowler reported striking improvement following this treatment in 69 per cent of recurrent cases of aerotitis carefully selected and controlled. He noted that after a single exposure to the radium applicator germinal centers disappeared and the number of lymphocytes was greatly reduced. The capillaries and fibrous tissue cells became more prominent. Several of the illustrations that follow were selected from his material.

Overexposure, in addition to reducing the lymphatic tissue, produces atrophy of the exposed mucous glands and scarring from the fibrous-tissue reaction, with possible stenosis of the auditory tube.

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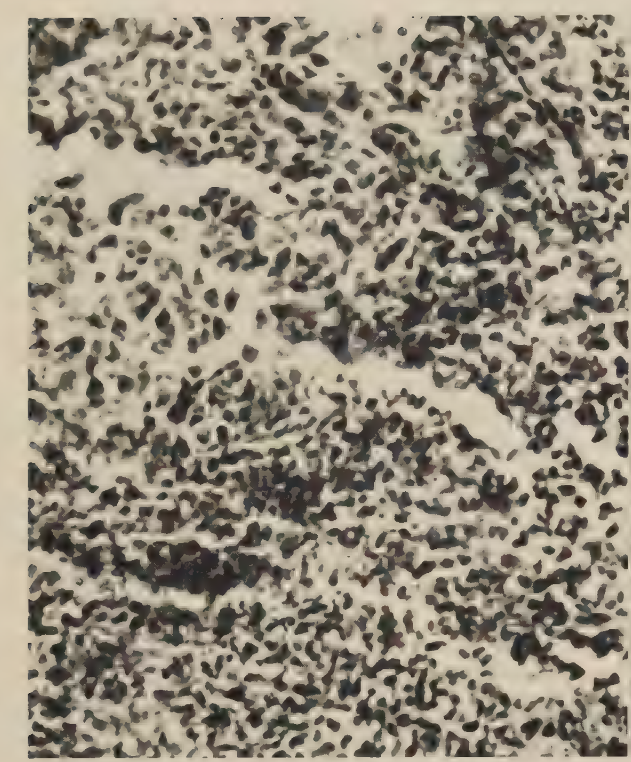
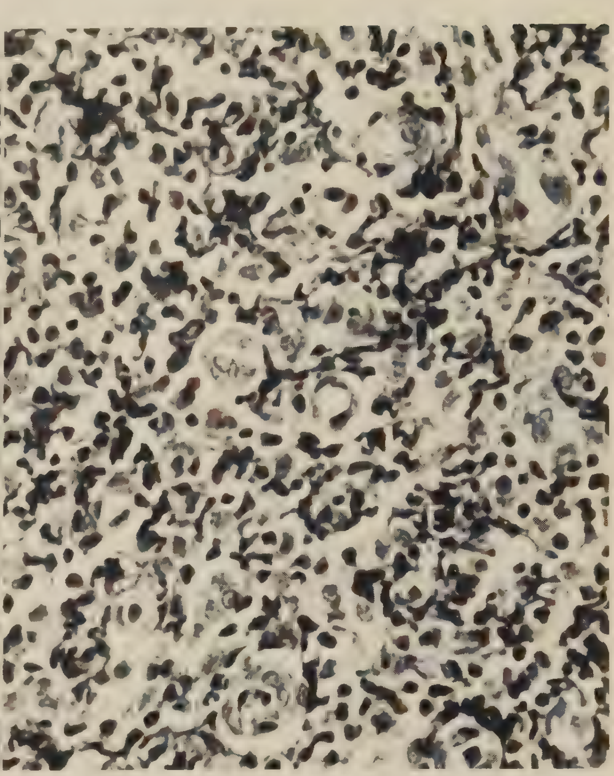
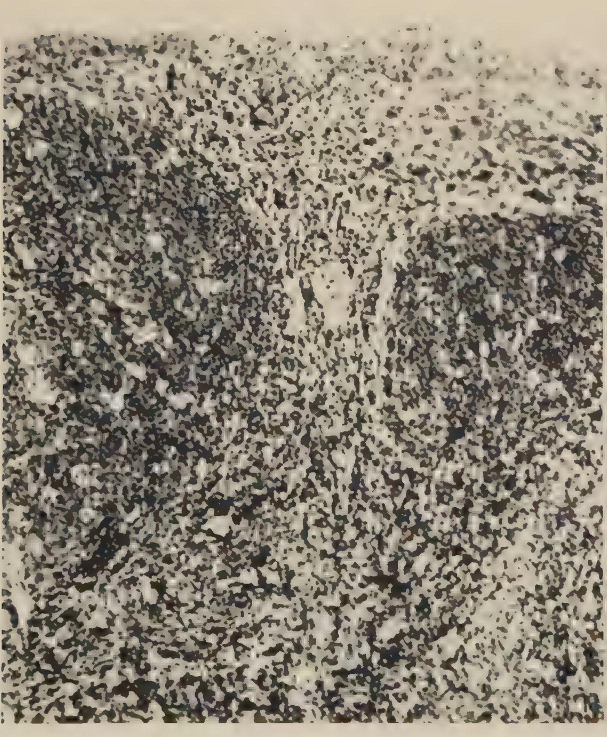


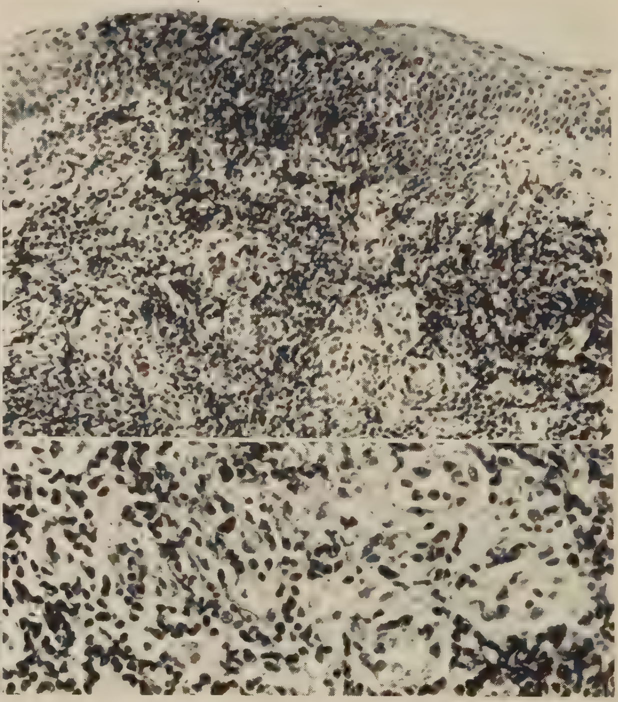
Lymphatic tissue, rich in lymphocytes, at mouth of eustachian tube of an aviator. x 500.



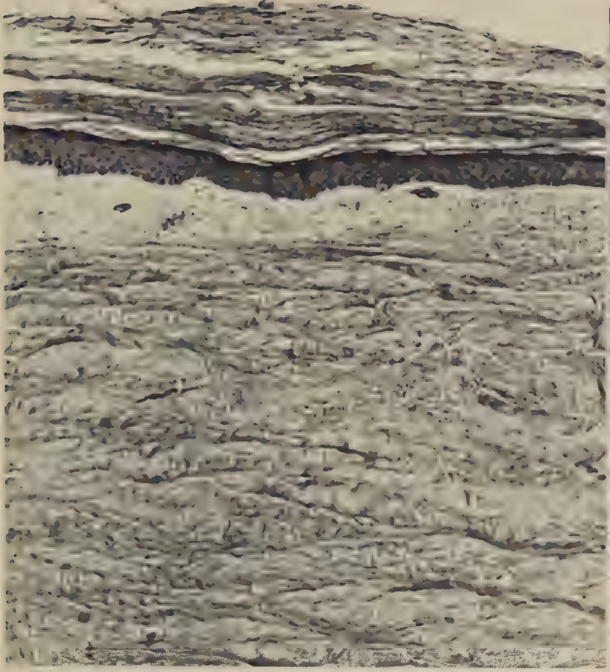
One month following 50 mg. hours exposure to radium in a 0.5 mm. walled platinum capsule, lymphocytes are diminished, reticuloendothelial cells and blood vessels are prominent. x 500. (Fowler).



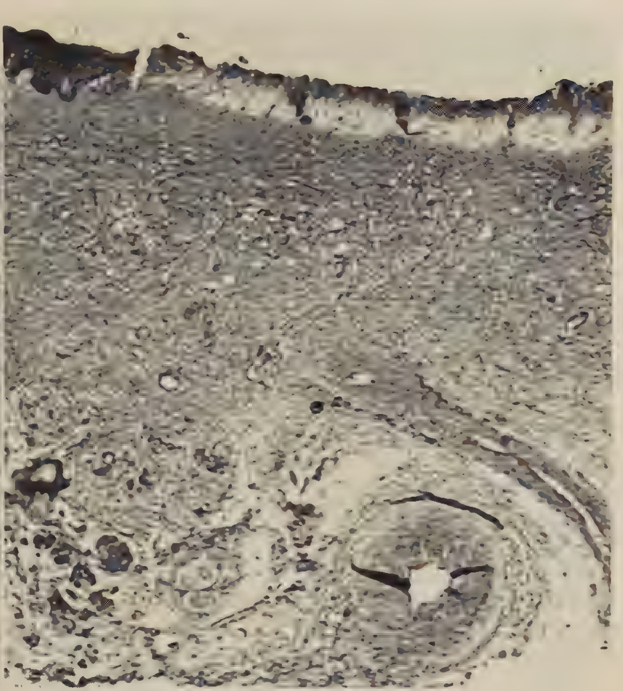
Normal adenoid showing dense primary lymphatic follicles in a thick layer of diffuse lymphoid tissue. Epithelium essentially pseudostratified columnar. x 125.



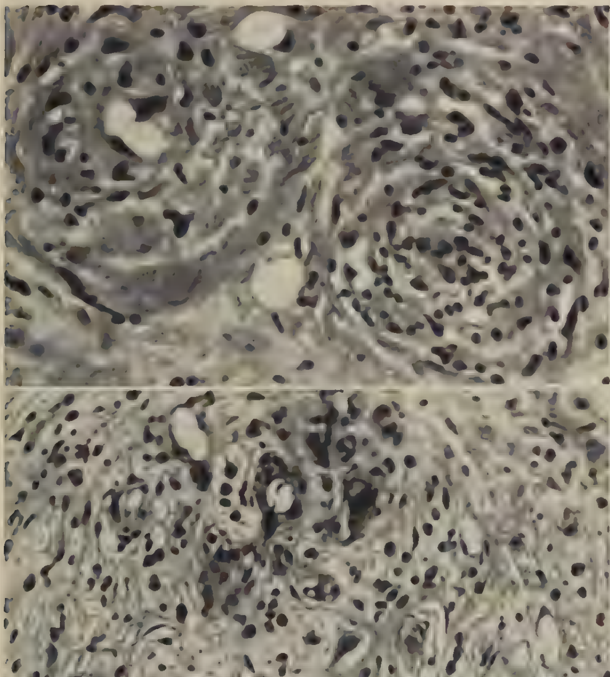
After exposure to radium, the follicles have lost many lymphocytes. Epithelium is stratified squamous. (x 125); reticuloendothelial cells and blood vessels are prominent (x 285).



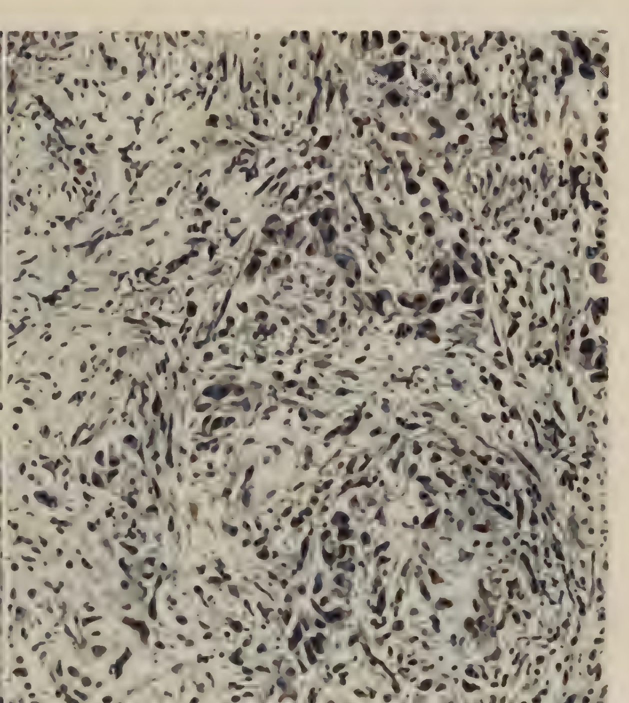
Irradiation effect, skin. Late result of therapy by million volt machine. Atrophy and keratosis of epidermis; absence of skin appendages; thickened inelastic relatively avascular, collagenized corium. x 55.



Roentgen-ray "burn," leg. Necrosis of epidermis; dense fibrosis of dermis; dilatation of superficial vessels, sclerosis of deep artery; scattered cellular infiltrate. x 25.



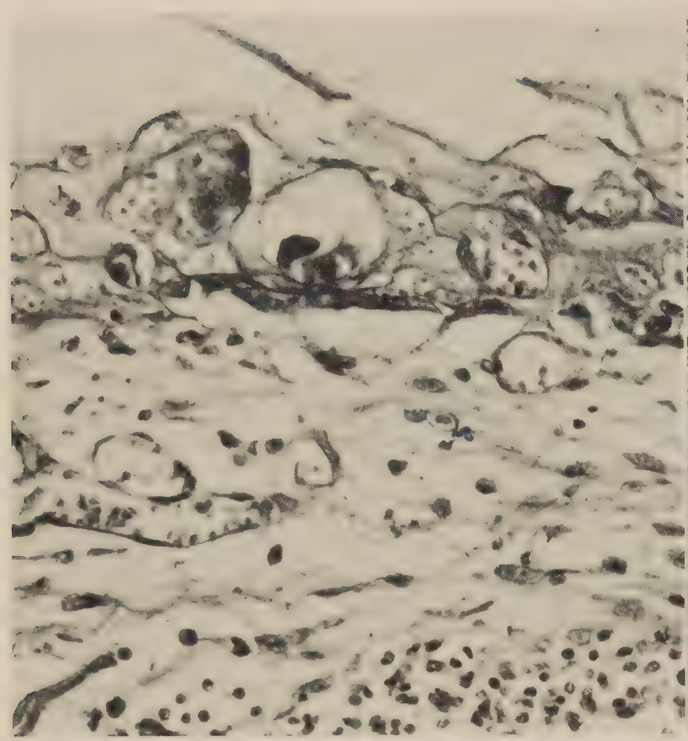
Details from case at upper right. **A.** Swollen small vessels with lumens obliterated (x 280). **B.** Atrophied sweat glands, and atypical fibroblasts with large, irregular, dark, nuclei (x 200).



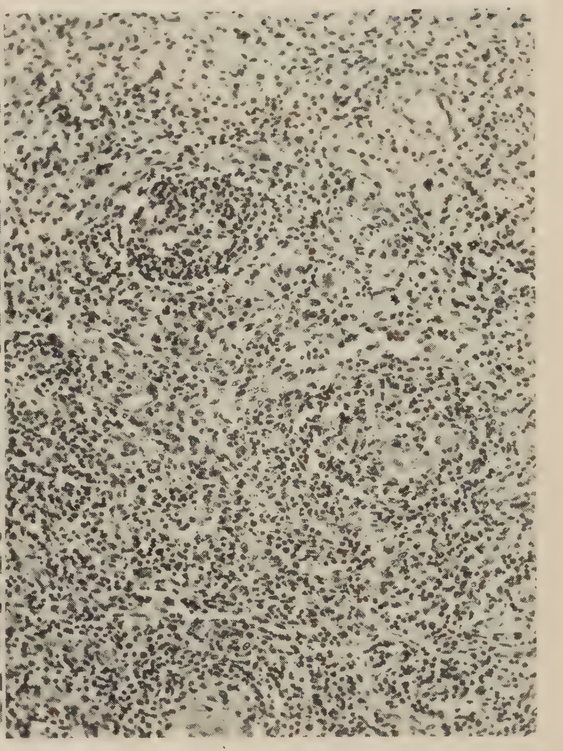
Carcinoma of epiglottis on 29th day after treatment. Few residual tumor cells in dense fibrous tissue. x 205. (At autopsy 6 months later, no tumor was found.)

IRRADIATION EFFECTS

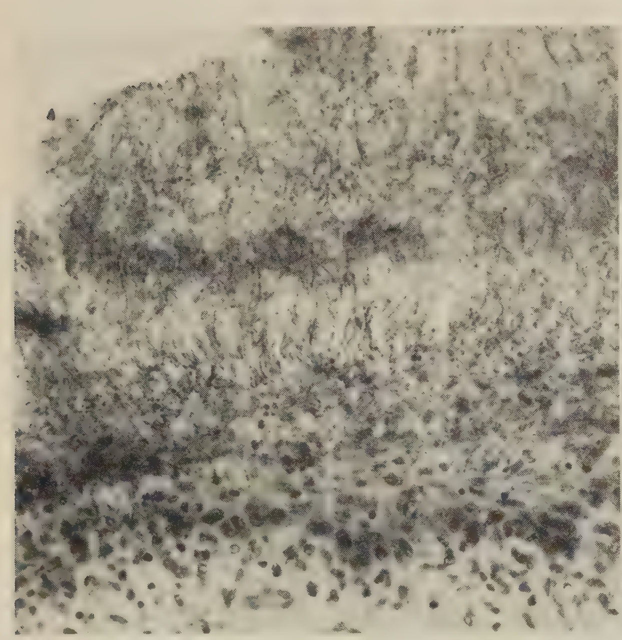
A-BOMB



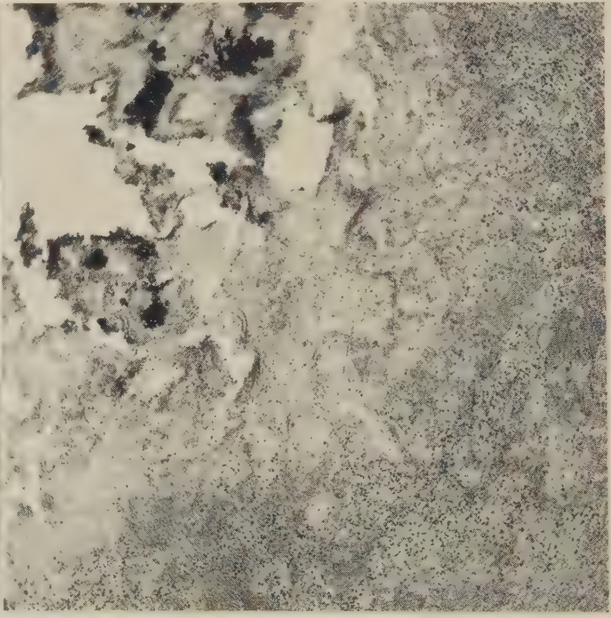
Pharyngeal mucosa of a young Japanese male who died on 10th day after explosion. Striking alteration of normal histologic structure. Bizarre hydropic degeneration of epithelium with clumped chromatin and desquamation of superficial layers. Markedly edematous stroma with dilated vessels, devoid of lymphocytes. x 450.



Lymph node of victim who died on the 24th day. Complete absence of lymphocytes and secondary follicles, but retention of fibrous structure. Proliferating reticuloendothelial cells, mononuclear cells of varying size, many atypical and bizarre forms, resembling cellular elements seen in malignant lymphoma. x 160.



Lung of same patient. "Necrotizing and hemorrhagic aplastic pneumonia" adjacent to necrotic tissue containing extensive bacterial colonies. Note virtual absence of leukocytic response. x 75.



Esophagus, proximal, of a woman who died on 30th day. Pseudomembrane composed of a fungus mycelium, probably monilial ("thrush"), firmly attached to basal layers of epithelium and invading at left. x 235.

Material from cases reported by Liebow, Warren and DeCoursey: Am. J. Path. 25:853-1027 1949.

CHAPTER 8

TUMORS

A few words concerning the general pathology and especially the histopathology of tumors will eliminate some repetition in considering neoplasms of the different anatomic parts. Squamous cell carcinoma of the lip has little morphologically to differentiate it from squamous cell carcinoma of the larynx or nose. Papilloma of the tonsil is generally similar to papilloma of any other squamous epithelial surface. It is these basic characteristics that will be mentioned and illustrated in this section. There are, however, clinical implications that depend on anatomic site more than morphologic features and these points will be emphasized in the sections dealing with special anatomic regions.

The character of benign tumors of epithelial origin is dependent on the type of epithelium involved. The only ones of squamous epithelium are the papilloma and the verruca.

EPITHELIAL TUMORS

Papilloma.—The papilloma is a tumor composed of both epithelium and vascularized connective tissue that extends beyond the normal level of the surface. The connective tissue furnishes the stalk to which the epithelium is applied. This connective tissue framework may be very delicate and branching or more robust and simple. The type of epithelium depends to some extent on that of the part involved. The squamous cell papilloma occurs most commonly on the tonsil, the palate, and in the larynx. It also occurs on the tongue and buccal mucosa but is rare in the nose. It occasionally develops in more than one site in the same individual. A few papillomas of the nose and sinuses are covered by columnar epithelium, and these cells usually secrete mucin.

Both the squamous cell and the columnar cell papillomas under discussion are benign, although occasionally one shows dyskeratosis. Such a tumor in the Registry had been removed from the anterior pillar of the right faucial tonsil of a 54-year-old man. It showed dyskeratosis of the leukoplakic type. A similar tumor was located on the opposite side near the lingual tonsil. In another Registry case a papilloma from the alveolar ridge of the mandible also showed dyskeratosis of leukoplakic type, and within a year frank squamous cell carcinoma had developed. The lesion, therefore, while generally benign, must not be regarded casually, especially in an older patient. This is particularly true of papillomas of the larynx.

The benign nature of the papilloma is indicated histologically by the regularity of the epithelium even when it is hyperplastic, and by the absence of detached nests of epithelium below its basement membrane. The limited amount of inflammatory reaction seen in the stalk is a result of traumatic irritation.

It must be remembered that the papilloma referred to here is to be segregated from the tumors showing papillary structure. Carcinoma of the nose and of the sinuses frequently grows with more or less of the papillary architecture. The epithelial papilloma of the nose is a special entity that is discussed in the section on that part.

VERRUCA VULGARIS, a clinical type of papilloma, is the common wart which is most frequently seen on the hands, particularly of young individuals. Of viral origin, it is very mildly contagious. It is a circumscribed papillary tumor, varying in size and contour in relation to the degree of papillation and the amount of keratosis that is always present to some extent. The surface is usually rough and fissured, and pink or darker in color. Verruca vulgaris occasionally occurs on the face, in the nasal vestibule, or much more often on the lips where it can be confused with the verrucous type of leukoplakia.

Histologically, like the papilloma, it is made up of vascularized connective tissue projections with overlying acanthotic and hyperkeratotic epithelium. Unlike the papilloma of the mucosal surfaces the papillations are not so delicate nor are they usually branched, but like the papilloma the basal layer is uniform and the maturation of the cells proceeds in a normal manner. There is no dyskeratosis and little if any associated inflammatory reaction in the underlying dermis. It is entirely benign. Histologically, there is little difference between verruca vulgaris and the venereal condyloma accumulatum. The latter is more frequently seen in moist warm situations, particularly at the mucocutaneous junctions of the anus and of the genitalia. The condyloma latum of syphilis may occur on the buccal and nasopharyngeal mucosa.

Adenoma.—The benign tumor of glandular epithelium is the adenoma. It represents an increase in the number of acinar elements that usually vary in size and cell content, but the epithelium is uniform in size and arrangement and usually sufficiently differentiated to carry on its specific secretory function. Adenomas can occur in any part of the mucosa and skin where gland elements are normally present. Many of the enlargements of glandular tissue, however, are not so much neoplastic as simply hypertrophic or cystic dilatation. Rhinophyma is an example of hyperplasia of sebaceous glands rather than a neoplasm, while adenoma of the thyroid is a true neoplastic process. Adenomas not infrequently include papillomatous hyperplasia of the epithelium, particularly if there is cystic dilatation of the gland elements. This is a common finding in the thyroid and in Warthin's tumor of the neck.

It is not always easy to differentiate between a benign and a malignant adenomatous tumor when there is variation in size and shape of the cells and indifferent or no acinar or tubular arrangement. This is particularly well exemplified by adenomas of the ceruminous glands in the external auditory canal and by tumors of the salivary glands. Tumors from both sources are commonly benign in spite of abnormal histologic features.

Carcinoma is a malignant tumor of either glandular or surface epithelium, and is basically of four classes–squamous cell (epidermoid), basal cell, transitional cell (lymphoepithelial), and adenomatous.

Carcinomas, with the exception of the basal cell tumors that do not metastasize, usually spread by way of lymphatics. As a group they are avascular and do not have the opportunity for dissemination by the blood stream that do sarcomas with their rich tumorous vascularity.

There are certain basic characteristics of malignancy applicable to tumors of any origin, from epithelium or mesenchymal tissues. First, rate of growth indicated by the number of mitotic figures. This does not necessarily indicate malignancy, for mitoses can be relatively abundant in epithelium, reticuloendothelium and other tissues that are simply responding to irritation. Atypical mitotic figures are the best single criterion of malignancy, excluding, of course, actual metastasis. Second, uncontrolled growth evidenced by anaplasia, the term applied to lack of differentiation and impairment of function. The mucous gland cell may not produce mucin, or it may do so in varying degree, even to excess. Third, invasion of contiguous tissues, and, fourth, metastasis to distant parts.

It must be remembered that any tissue growing abnormally, either as a result of irritation or of neoplastic influence, is potentially malignant, even if only remotely so. Further, histologic features are frequently misleading. Lesions such as dermatofibroma, blue nevus, pseudoepitheliomatous hyperplasia are disturbing cytologically but clinically benign. On the other hand, an innocent appearing fibroma, adenoma of the thyroid, or mixed tumor of a salivary gland, may eventuate in metastasis. These are possibilities that make the experienced pathologist dubious of the dependability of tumor grading and certainly of the unreserved diagnosis of malignancy by the popular cytologic method.

Squamous cell carcinoma arises from the squamous epithelium of the skin and mucosae and from other epithelium by metaplasia. It is characterized by the invasion of underlying tissues by strands and islands of epithelial cells that can usually be identified as of squamous origin even if the tumor is of a high grade of malignancy. There is a cohesiveness among the cells, and somewhere in the tumor the tendency to differentiate to the squamous type will be found, even though the prickles and keratin seen in the more mature cells are absent. The nucleus of the squamous carcinoma cell is generally large, vesicular, and possesses a very prominent nucleolus which imparts to the nucleus its "bird's eye" character. In the more differentiated tumors, groups of cells are seen in which normal maturation and keratinization have progressed to the point of producing the characteristic epithelial "pearl." This must be distinguished from the keratin cyst seen in such benign skin lesions as seborrheic keratosis. These details are illustrated in the following plates.

In less differentiated tumors the cells become spindle in type and mimic those of a very cellular connective tissue tumor, or the cells are large, bizarre in shape, and at times multinucleated. Multinucleated giant cells are not as common, however, in carcinomas as they are in sarcomas.

Basal cell carcinoma is specifically a skin tumor that will be discussed and illustrated in detail in the section dealing with nevi.

Transitional cell carcinoma or lymphoepithelioma.–The first of these terms is not good because it is applied to the group of tumors arising in the urinary tract. The normal urothelium is also of undifferentiated type and the common papilloma arising in the urinary mucosa retains that form, as do the majority of the frankly malignant tumors of that region. The term lymphoepithelioma is likewise unsatisfactory because only a small percentage of the tumors retain the epithelial and lymphatic tissue elements. If the term be retained, it should be applied only to those tumors arising from the mucosa of the pharynx, particularly of the nasopharynx. These terms are retained here, however, in deference to their long use and as an introduction to the suggestion of a new and more appropriate terminology. Neither is it considered that the term squamous cell carcinoma is adequate, in spite of the fact that the tumor is so frequently epidermoid or shows some areas of attempts so to differentiate. The majority of these tumors, however, especially those in the nose and sinuses, show no such specialization but are characterized by a wide range of cell forms and architecture which cannot be implied by the term squamous cell carcinoma. Actively proliferating respiratory epithelium has a tendency to grow as undifferentiated epithelium, but since it is derived largely from ectoderm, any differentiation is generally toward the squamous type. This occurs not only when the epithelium is growing as a tumor, but also as a result of chronic irritation. This abnormal squamous epithelium undergoes dyskeratosis and frank malignant changes just as does the epithelium of the skin and mucosae where epidermal epithelium is normally present. It is not surprising, therefore, that carcinomas of the respiratory epithelium frequently exhibit the squamous cell tendency.

The close association between epithelium and lymphatic tissue seen particularly in the mucosa of the nasopharynx is either a genetic relationship or the result of an inductive effect of one tissue on the other. According to Willis, this need not be considered a factor influencing specialization of tumors from such epithelium. He considers all of the carcinomas arising from respiratory epithelium, therefore, squamous cell tumors. Experience, however, makes one hesitate to accept this simplification. There are definite differences in the behavior of carcinomas arising in the upper respiratory tract and of those arising in epithelium elsewhere.

This discussion is amplified and illustrated under malignant tumors of the nose, paranasal sinuses and nasopharynx at the end of the section covering these parts.

MESENCHYMAL TUMORS

The benign tumor of mesenchymal origin is a focal neoplastic hyperplasia of a specific element that arises from the embryonal mesodermal layer and that tends to retain the characteristics of the tissue of origin. Tissues that arise from the mesoderm include fibrous connective tissue, fat, smooth and striped muscles, cartilage, bone, and vascular elements. It is usually possible to identify the histogenesis of the tumor even when it springs from such comparatively undifferentiated tissues as smooth muscle and fibrous connective tissue. The nature of those from the more highly developed tissues, bone, cartilage and blood vessels, is more evident. It is not always easy, however, to differentiate simple hyperplastic reaction to inflammation from neoplastic proliferation. Granulation tissue, for example, may be so cellular and the cells, including giant cells, sufficiently pleomorphic as to mimic not only benign fibroma but fibrosarcoma. It is very difficult at times to differentiate callus from osteoma or chondroma. Neoplastic proliferation generally shows less tendency to purposeful structure than reparative hyperplasia, and the cell arrangement is usually not so orderly. In chondroma, for example, the chondrocytes vary in size, the lacunae in which they lie are generally less uniform in size, and there may be two or more cells in one space. The intercellular chondromucin varies in character and distribution, while in hyperplastic reparative proliferation these variations from the normal are usually at a minimum.

All connective tissue tumors are made up of two elements, cells and intercellular substances. In fibroma the latter is fibroglial fibrils and collagen, in chondroma it is chondromucin, and in osteoma it is osteomucin which has the specific characteristic of attracting calcium.

Fibroma.—The proportions of fibroblasts and intercellular substances making up a fibroma vary considerably. The cells generally are spindle shaped with a limited amount of obvious cytoplasm, the nuclei are ovoid and their size and chromatin content vary with rapidity of growth. In young, rapidly growing cells the nuclei are more vesicular and much larger. In older, slower growing tumors the nuclei are attenuated and the chromatin is more concentrated. Fibrils extending from the ends of the cells are best seen by special stains. Generally, the cells and their fibrils are arranged in interlacing fascicles. In the rapidly growing tumor there may be no obvious collagen, but there usually are areas with loosely arranged cells, some of stellate rather than spindle shape, and an accumulation of fluid. Tissue of this type is called myxoid. In neurofibromas the term Antoni B is applied to such tissue to distinguish it from the more cellular and fibrillar portions, Antoni A. When the bulk of the tumor is made up of this mucoid material it is called a MYXOMA. This generally indicates a more rapidly growing and a more malignant tumor.

There is now little argument that the simple polyp of the respiratory mucosa is not a true neoplasm of connective tissue, but that the connective tissue cells present are part of the chronic inflammatory reaction. It has, however, been called FIBROMA MOLLUM. Other fibromas show a marked scarcity of fibrocytes, a preponderance of collagen, and a sparsity of blood vessels. Such a tumor is called FIBROMA DURUM. It is the common form seen in the buccal mucosa and it is the final stage of the nasopharyngeal fibroma.

The KELOID is a striking example of this “hard” type. There are two clinical forms: the primary, developing without a history of previous injury, and the much commoner secondary, developing in response to an injury that may be trivial. It occurs most consistently in the dark-skinned races. It proved to be a serious problem in the Japanese injured by the atomic bomb.

Histologically, keloid consists of broad bands of collagen that replace the normal collagen of the dermis. It is practically avascular and poorly cellular. It may seem strange that with no histologic evidence of cell activity the tumor should grow so persistently. Since our knowledge of intercellular substance has developed this becomes more understandable, and there is justification for considering keloid a neoplasm of colloid. It is difficult to eradicate by excision because the additional trauma incites further collagen formation. Irradiation seems to be a more satisfactory treatment.

Neurofibroma.—There is still controversy as to the histogenesis of the fibrous tumors of nerves, whether they arise from the connective tissue elements of the nerve sheaths, from the cells of the neurilemma, or from both. The perineurium and epineurium are probably mesodermal, so a tumor arising from them would be a neurofibroma, while the neurilemma is neuroectodermal in origin and contains the cells of Schwann. Tumors from these cells are called schwannomas or neurilemomas. Stout is a firm advocate of this origin of the circumscribed, encapsulated tumor of nerve fibers and reserves the term neurofibroma for the more diffuse tumor encountered most commonly as the multiple neurofibromatosis of von Recklinghausen's syndrome.

Histologically, the chief point of differentiation between the neurofibroma of connective tissue origin and the neurilemoma of neuroectodermal origin is evidence in the latter of attempts to form specialized neural elements, such as tactile corpuscles. The nuclei of the neurofibroma are so generally palisaded as to be a distinguishing histologic criterion, and it may be to the extent of producing the *formes frustes* of specialized neural elements, described by Verocay, that are called Verocay bodies. This is one reason that some do not attempt to differentiate the two types of tumors, but call them both neurofibromas.

The NEURILEMOMA, consistent with its origin in the neural crest, may contain melanocytes and nerve cells. The latter are prominent in peripheral neurocytomas or ganglioneuromas.

The common tumor of the 8th nerve is an example of the more diffuse neurofibroma as seen in the von Recklinghausen syndrome and is, at times, an element in that syndrome.

Myomas are of two groups, leiomyoma arising from smooth muscle, and rhabdomyoma arising from voluntary striped muscle. Both tumors arise usually in sites where the respective muscles are normally present. The most common sites, therefore, for LEIOMYOMA are the uterus, the musculature of the gastrointestinal tract, and the skin. It may also arise from the musculature of blood vessels, when, in addition to the smooth-muscle cells, the tumor will include the vascular element. It occasionally arises in areas where non-striped muscle is not ordinarily found. An example of this in the Registry is a tumor removed from the tongue of a 39-year-old man. It had been present in the median line of the dorsal surface of the tongue since birth and was painless.

With the exception of those of vascular origin and those of the skin, myomas are circumscribed. Those of the skin are usually more diffuse, and those of blood-vessel origin, the hemangiomyomas, are actively invasive.

The myoma is made up of interlacing bundles of spindle cells that have vesicular, oval nuclei and fairly abundant cytoplasm tapering off at each end. Myoglial fibrils can usually be demonstrated by special stains. These are characteristically along the side of the cells rather than extending directly from the pointed ends, as do fibroglial fibrils in fibrous connective tissue. A variable amount of connective tissue stroma supports the muscle bundles. The tumors are generally poorly vascularized. They can be distinguished from fibromas by the larger amount of cytoplasm in the individual cell, the position of the fibrils, and the scarcity of collagenous intercellular substance. The relatively larger amount of cytoplasm is evident in cross section of the bundles where the cells look like small round cells with centrally placed nuclei. This is an important identifying feature.

Leiomyoma of the skin arises from the arrectores pilorum, is characterized clinically by being very tender and by giving rise to paroxysms of unprovoked pain. It appears as a collection of papular lesions or a more diffuse single tumor. It is not uncommon on the face.

RHABDOMYOMA is of more importance to the otolaryngologist because a common site is the tongue. The benign and malignant forms of this tumor are usually not as sharply defined as are those of smooth muscle. The distinction is largely academic and depends on the attempt to interpret the degree of pleomorphism in the cells. The tumor is rare in any form, and those in which the muscle fibers are well differentiated are extremely so. One of the very suggestive characteristics of the tumor is the great variation in size and shape of the cells. They occur as large ribbons of cytoplasm and large round cells, either of which can have one or more nuclei. The majority of the cells, however, are small undifferentiated spindle forms. It is only by the demonstration of cross striations that the tumor can be definitely identified. These tumors may grow to large size, recur persistently after attempts at surgical removal, but even the most histologically malignant ones, certainly those of the tongue, rarely metastasize.

Chondroma.—There are two types of chondroma: enchondroma that arises within cartilage or within bone that develops from cartilage, and ecchondroma that develops from the perichondrium. There is considerable difference in the clinical behavior of these two tumors. The enchondroma occurs most commonly in the bones of the fingers and toes, where it produces an expansile lesion that is mechanically troublesome but is rarely malignant. The ecchondroma arising about the joints is usually benign but occasionally is malignant.

Histologically, each of these types is a duplication of the normal cartilage in respect to content of chondrocytes and intercellular chondromucin, but these elements are disposed in a less orderly pattern. It is not uncommon to find trabeculae of bone developing in the cartilage. In the malignant tumor (CHONDROSARCOMA) the cells may lose their identity and appear as undifferentiated spindle cells. The chondromucin may be entirely absent or in such small streaks as to be unrecognizable. In other portions of a tumor it will be present in a watery or mucinous state, scarcely taking the basic stain for normal chondromucin.

The tumors arising from fibro-elastic cartilage are more cellular and usually have less chondromucin than the tumors arising from osseous cartilage. The cells may show fibrils like those of fibroblasts. There are no lacunae and the cells exhibit none of the palisading that is characteristic of enchondral bone just before it ossifies. This tumor is less aggressive than those arising from enchondral bone. It is the type that usually develops on the nasal septum, occasionally in the larynx and external auditory canal.

Chondroma is rare in the respiratory tract and, according to Lugli, seems to be more common in the ethmoidal region than in other portions. Here it can be a serious affair even though it is benign, because it grows aggressively though very slowly over a period of years and destroys the bones by pressure, so that it eventually invades the nose, orbit, and cranial cavity. Because of its location it is difficult to remove surgically and it is not particularly sensitive to irradiation; therefore it recurs persistently. In its earlier stages it must be differentiated from mucocele of the sinus. It more often becomes clinically evident through involvement of the orbit than by nasal obstruction.

The site of chondromas probably depends on the location of the enchondral ossification centers of the bones. For this reason also it develops more commonly in younger individuals, although because of its very slow growth it may not become evident until much later in life.

The Registry contains several cases of chondroma originating in the nasal septum. One reported by Howarth in a 35-year-old man produced expansile deformity of the nose. Chondroma of the larynx is found more frequently in adult males. It usually arises from the cricoid or thyroid cartilage.

Cartilage develops in other tumors that do not originate in cartilage and bone, particularly in the mixed tumor of the salivary-gland type. A mixture of osseous and cartilaginous elements is common in bone tumors—osteochondroma—especially in those that arise in the ethmoidal region of the nose.

Osteoma in the nose and sinuses is a tumor of mature bone arising from the osteogenic periosteum of the bony walls. It is benign, grows very slowly, and often remains clinically silent until it has reached such proportions that it produces symptoms of pressure or obstruction. It is not infrequently discovered incidentally during an x-ray survey of the head.

Like chondroma, its development begins in early life when osteogenesis is most active. It is more common in the frontal sinus than in any other portion of the respiratory tract, with the largest number in the recessus nasalis and along the suture between the ethmoid and frontal bones. In the ethmoidal sinus it may arise from that aspect of the ethmofrontal suture. Those that present in the maxillary sinus or in the sphenoidal sinus usually develop along the border of the ethmoid bone.

The rarer primary intranasal osteoma usually springs from a turbinate, particularly the inferior. It occurs more commonly in the external auditory canal. A number of the osseous lesions in the external auditory canal are probably exostoses rather than neoplasms. Lesions of this description occur most commonly deep in the external auditory canal.

Osteomas occasionally develop in or on the mastoid process. In the latter case, there will be a hard, rounded subcutaneous deformity behind the ear.

Tumors arising in the nose or sinuses may produce external deformities, most characteristically a bulging of the base of the nose that results in the “frog face” effect, or sometimes as a horn over the frontal sinus.

Histologically, osteoma mimics in architecture and histologic detail adult cancellous bone, but there are variations in the proportion of dense cortical and trabeculated cancellous components. It is usually a smooth, rounded excresence with a firm capsule of cortical bone and a core of loosely cancellous type, or it is composed entirely of dense eburnated bone having narrow haversian canals. The tumor may have a broad base or it may be pedunculated. Occasionally it becomes completely detached and acts as a loose foreign body in a sinus. Discussion of other osteogenic tumors will be found in the section on tumors of the nose and sinuses.

Xanthoma.—The respiratory tract is occasionally involved in a general xanthomatosis that produces yellowish brown plaques or masses, especially in the larynx, but also in the mucosa of the mouth, pharynx, and trachea. These are deposits and not neoplasms. Xanthelasma of the eyelids is one clinical form. It occurs in the older age group and may be associated with atheroma of the coronary arteries and aorta. Xanthoma tuberosum multiplex is another. It occurs in younger individuals and at times is associated with diabetes mellitus.

The deposits are made up of foamy endothelial cells and a special giant cell (Touton) which is readily distinguishable by the arrangement of the nuclei in a circle near the periphery of the cytoplasm, and by the corrugated character of the cell surface. Special stains identify cholesterol or other lipids in the cytoplasm.

The various xanthomatoses are the result of a disturbance of fat metabolism in which there are focal deposits of lipids that are taken up by endothelial cells to form the clinical lesions. While the condition is a general disturbance, there must be some local factor that determines the distribution of the deposits. The nature of this is not known.

Myoblastoma is a rare tumor, if indeed it is a neoplasm. It is of interest to the otolaryngologist and oral surgeon, for it develops most frequently in the tongue and the lips, occasionally in the gingivae as the congenital epulis, and at times in the larynx. The tumor occurs at any age, shows a slight predilection for the male, and is quite without symptoms. It seldom reaches a size larger than that of a small pea. It is benign; in fact, it shows little evidence of any growth activity.

Its histogenesis is still a matter of dispute. It was rather generally accepted originally to be an embryonal stage of muscle cells that through some dysontogenesis remained immature. That theory is responsible for the name of the tumor which was first applied to it by Abrikossoff. Horn and Stout later wrote of the condition and indicated their belief that the tumor did arise from aberrant myoblastic rests. Another theory is that they are degenerative forms of injured striped muscle fibers. The cells, however, do not resemble particularly the myoblast as seen in the embryo, nor do similar cells appear in the destruction and repair of striped muscle.

The tumor was originally described in the tongue where there was thought to be a direct association with the muscle fibers, but tumors made up of the same type of cell have been described in the skin and the breast where striped muscle is not normally present. There is no evidence in the tumor of maturation to striped fibers.

The theory that the cells are neurogenous was recently advanced by Fust and Custer. They were able to demonstrate cells similar to those of myoblastoma in nerve twigs well beyond the limits of the obvious tumor. Neural elements were present in the thirty-six cases that they studied. Their theory has received support from Bangle in a morphologic and histochemical study of 43 such tumors from tongue, skin, lip, breast, vocal chord, and floor of the mouth.

The cells are characteristically uniform in size, shape and structure, somewhat resembling xanthoma cells. They are large, granular, and not vacuolated. The granules are neutrophilic, and the cytoplasm does not contain fat but it is rich in glycogen. The nuclei are small, usually centrally placed, and with concentrated chromatin. Mitotic figures are rarely if ever observed. The cells are arranged in small clumps by delicate connective tissue septa. When the tumor is in close proximity to the epithelium, as it usually is in the tongue, the epithelium is practically always hyperplastic, even to the extent of being pseudocarcinomatous.

Whatever the histogenesis, the cell masses are a specific entity. If the term myoblastoma is to be retained, however, it should be thoroughly understood that it refers only to this lesion and not to tumors that are obviously of muscle origin, some of which are frankly malignant. Several instances of metastasizing myoblastoma have been reported. There is a question as to whether these really are of the same histogenesis and not from organoid mural elements.

Sarcoma.—All of the mesenchymal tumors have a malignant form: fibrosarcoma, chondrosarcoma, osteogenic sarcoma, etc. The histologic criteria of malignancy are, first, active growth evidenced by the presence of mitotic figures, but, of more significance, mitotic figures that are atypical in the number and character of the spindles; second, variation in size and shape of the cells; third, tumor giant cells; fourth, absence of or sparse evidence of differentiation of cells to any specific type of adult tissue, and fifth, character of the vascularity. Mesenchymal malignant tumors are usually well vascularized but the blood vessels are poorly developed; some are without organized walls, existing simply as blood channels lined by tumor cells. Clinical and histologic evidence of invasion of surrounding tissues and of metastasis to distant parts, especially the latter, are really the determining points for malignancy. It is a frequent and confusing feature of mesemchymal tumors, however, to appear malignant histologically yet to behave clinically as benign. As a rule, benign tumors are encapsulated or at least circumscribed in growth rather than invasive.

ANGIOMAS

Angiomas may be of a variety of types in addition to the natural division into hemangiomas and lymphangiomas. The following remarks refer to the much commoner and more variable hemangioma, unless otherwise stated.

The tumor has a variety of forms. The simplest consists of a mass of more or less well organized vessels with little or no excess of any of their cellular components. It is sessile, not circumscribed, and if superficial, the cirsoid character of the vessels may be seen. When the vessel lumens are prominently dilated the tumor is referred to as cavernous angioma. One vessel may become sufficiently dilated to be mistaken for a glandular cyst. The vessels are usually formed of normal adventitia, media, and endothelial intima, and sometimes lymph vessels can be differentiated from blood vessels only by their contents. The tumors of this type are hamartomas and are not truly neoplastic. A HAMARTOMA is a local accentuation of one or more elements normal to the part. A well known example is the cavernous hemangioma of the liver. A CHORISTOMA, on the other hand, is the presence of elements in a situation where they are not normally present, ganglioneuroma of the nose, for example.

Other vessel tumors are complicated by neoplastic proliferation of one or more of the vessel elements. This may be of the lining endothelium, when the tumor is termed HEMANGIOENDOTHELIOMA, or of the smooth muscle and other cellular elements of the adventitia, when it is called HEMANGIOMYOMA. This group includes Stout's PERICYTOMA.

Vascular tumors may be restricted in extent, increasing in size chiefly by dilatation of the lumina, or they are aggressively invasive, especially along fascial planes, when they are very difficult to eradicate surgically. These are seen most commonly in children; they are usually made up of much smaller blood vessels, and there is usually an increase in the endothelial or perithelial elements.

Only rarely has a report been made of a hemangioma that has metastasized. The malignant hemorrhagic sarcoma of Kaposi is an entirely different disease and is always fatal.

The hamartomatous angioma is more common in the tongue, lips, and tonsils than in the respiratory tract. The common, very vascular lesion of the larynx—the laryngeal nodule—is not a hemangioma. The proliferation of blood vessels in these lesions is not neoplastic. The dilatation of the resulting thin-walled vessels produces the varix stage. (See in section on the larynx.)

HEMANGIOMAS OF THE NEVOID TYPE may be associated with similar lesions in situations other than the skin; for example, the Lindau syndrome that includes angioma in the choroid of the eye and cysts and hemangiomas of the brain, especially the cerebellum. These are congenital tumors and are made up of any type of blood vessels from capillaries to those with well organized walls. They are generally flat and circumscribed, or nodular like the septal hemangioma. It is difficult to identify them histologically as congenital nevi except by the history and the clinical picture. Hereditary hemorrhagic telangiectasia is a clinical form of this type. It is an inherited condition in which the lesions may appear in any part of the body but are commonly found in the nasal and oral mucosae. The multiple and often severe epistaxis that results may be difficult to control. There is a predilection also for the skin of the face.

The other clinical types of focal hemangioma—GINGIVITIS GRAVIDARUM (PREGNANCY TUMOR) and GRANULOMA PYOGENICUM are indistinguishable histologically. The former appears in about 2 per cent of pregnancies in the first few months and usually recedes after parturition. This suggests a hormonal influence in its etiology. Occasionally it persists for months after termination of the pregnancy. The entire gingiva may be involved in the red, swollen, bleeding process, and it may be a very annoying complication refractory to any treatment except termination of the pregnancy. Occasionally the reaction is limited to a local tumor projecting from either the buccal or lingual surface of the gingiva, the pregnancy tumor. While predominantly a gingival lesion, there is in the Registry one specimen removed from the nasal septum at the usual site of the septal hemangioma, and another that was removed from the palate several months after the patient had been delivered. Incidentally, this patient had had a similar experience during a previous pregnancy.

Histologically, the lesion consists of a mass of blood vessels, beginning as well formed and large ones in the base and terminating as a mesh work of capillaries at the surface, supported by a loose fibrous tissue stroma infiltrated with exudate that includes granular leukocytes when the surface is ulcerated. A common feature is hyperplasia of the associated surface epithelium.

GRANULOMA PYOGENICUM is a small well circumscribed, ulcerated, bleeding papule occurring on the fingers, lips and mucosae. It is resistant to treatment and must be excised completely to avoid recurrence.

It resembles the pregnancy lesion in vascular content and stroma, but the exudate always includes granular leukocytes. Hyperplasia of the epithelium is not as prominent a feature as it is in the pregnancy tumor.

A third important clinical entity in this category is the HEMANGIOMA (BLEEDING POLYP) OF THE NASAL SEPTUM, which is discussed with the benign tumors of the nose.

Of special interest to the chest surgeon is the congenital arterio-venous anastomoses in the lungs that have become increasingly evident since the development of angiocardiographic technique.

As a class, hemangiomas, particularly the actively growing ones, are comparatively sensitive to irradiation. Electrolysis and simple excision may be used for some of the smaller ones and excision and skin grafts for large ones.

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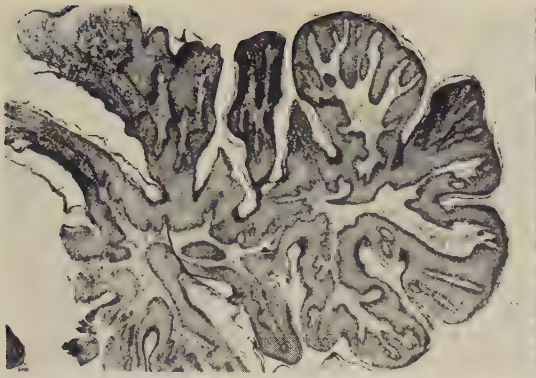
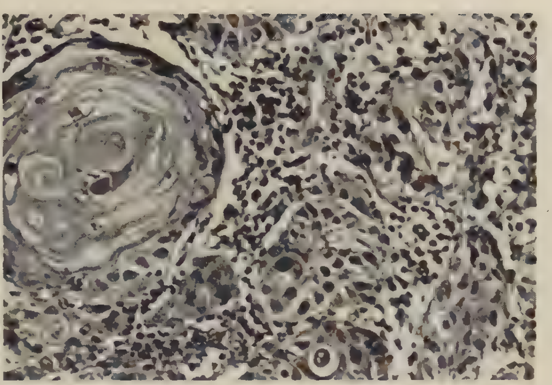
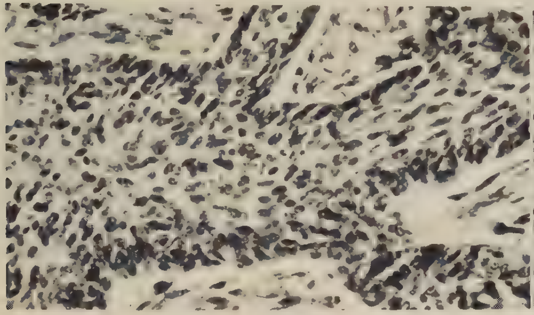


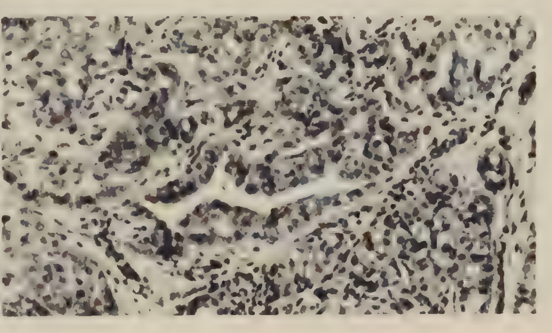
Papilloma, external auditory canal. Branching core of vascular fibrous tissue covered by well organized squamous epithelium. Benign. x 16.



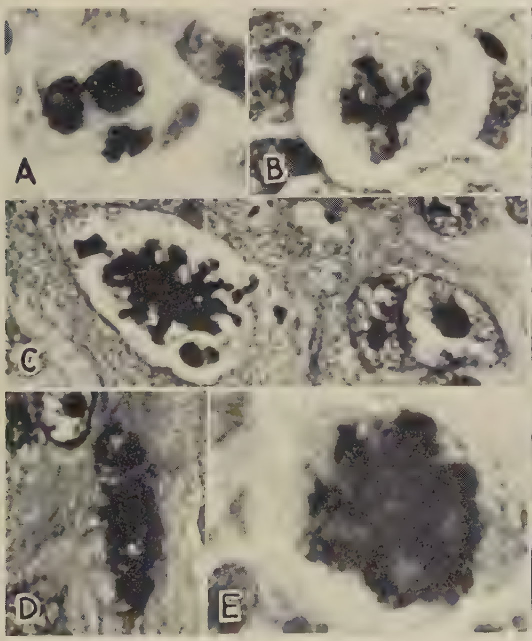
Squamous cell carcinoma of tongue. "Epithelial pearl" (at left): concentrically arranged, partially keratinized cells surrounded by less differentiated squamous cells. x 150.



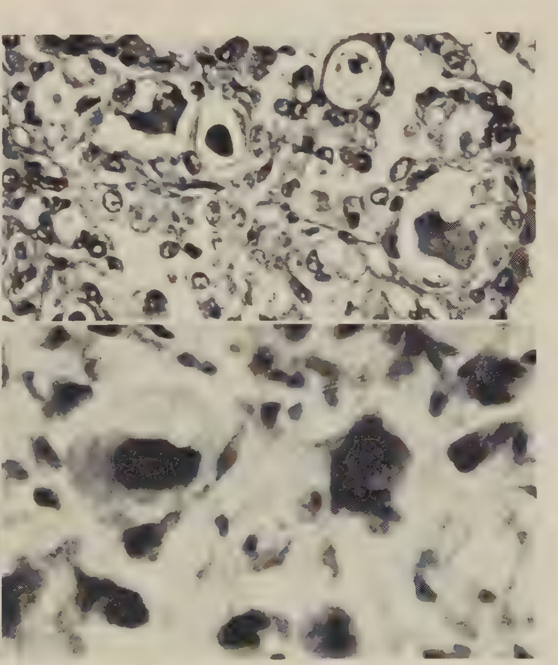
Basal cell carcinoma, ear. Uniform, oval, hyperchromatic cells resembling those of basal layer of epidermis and hair follicle, with outer row of vertically palisaded cells. x 165.



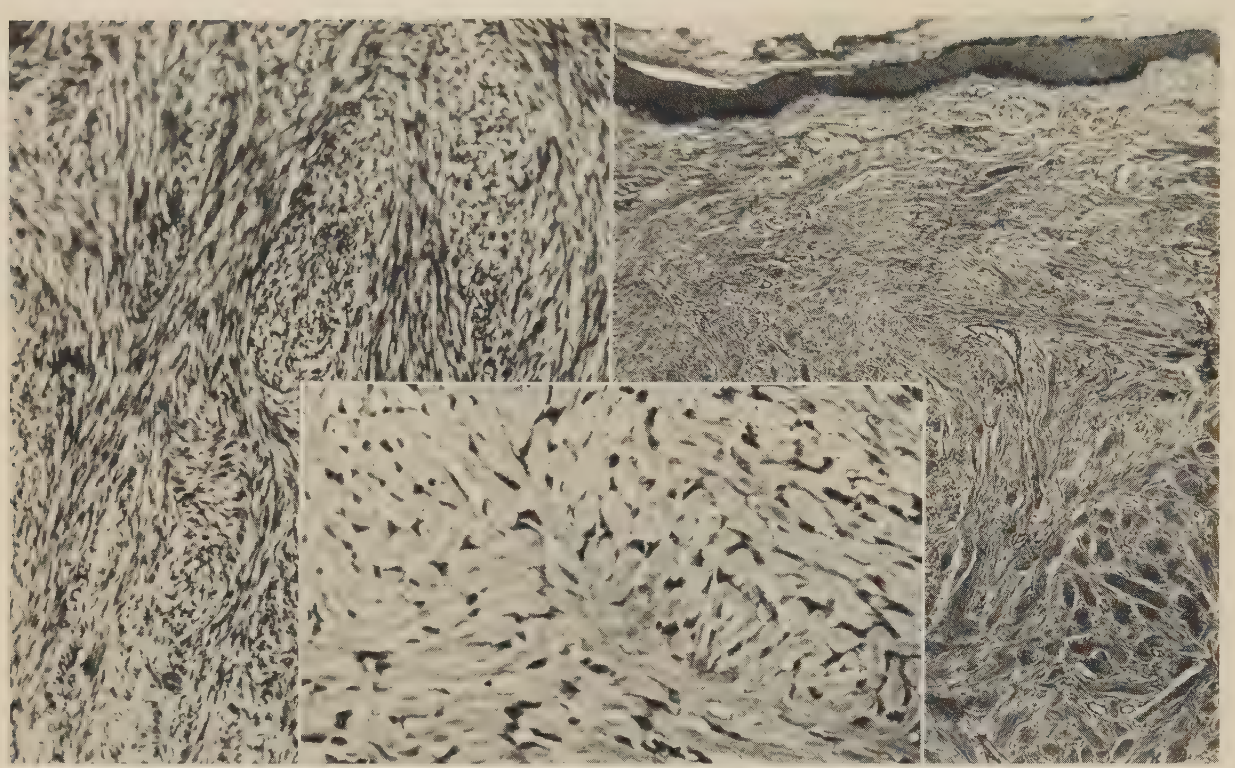
Adenocarcinoma, palate. Cells, cuboidal or columnar, showing attempts to form gland acini. Small groups are invading independently. x 145.



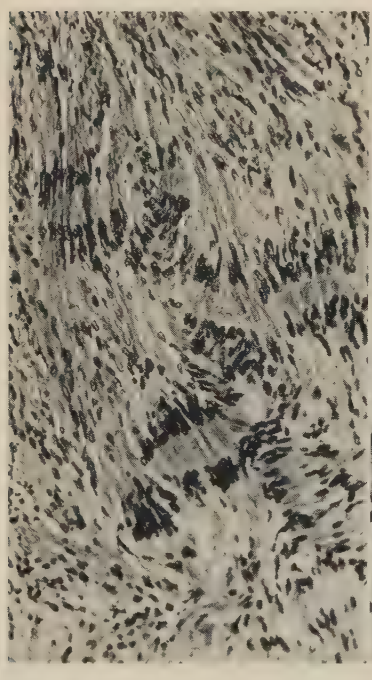
Atypical mitoses: A. Tripolar (x 1300). B. Quadripolar (x 1000). C. Multipolar mitotic figure and a "bird's-eye" nucleus (x 800). D. Irregularly chromatinized metaphase. (x 800). E. Giant nucleus in multipolar mitosis (x 1300).



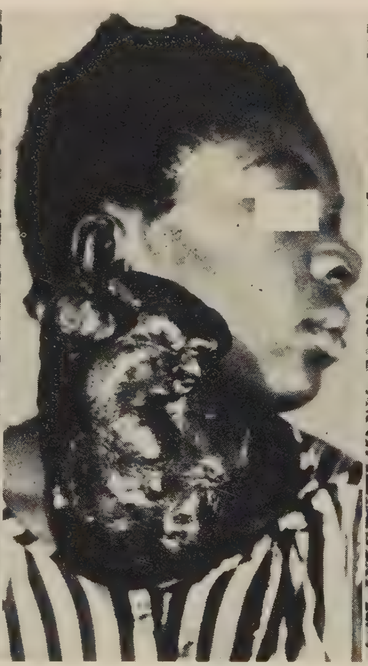
Examples of pleomorphism. Varied cytologic abnormalities in size, shape, nuclei, and cytoplasmic features. x 450, x 680.



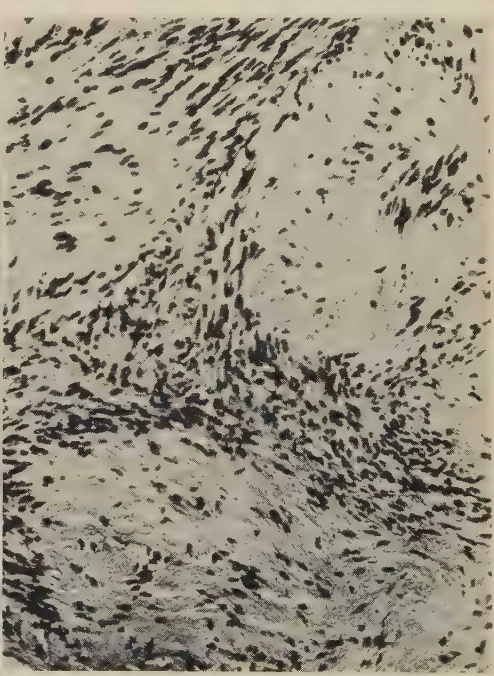
Fibroma. A. Interlacing fascicles of relatively uniform spindle cells, benign. x 125. B. Keloid. Pale thick strands of poorly cellular collagen replacing normal collagen of dermis, a small amount of which may be seen. x 60. C. "Hard" fibroma. Predominantly collagen strands; cells dispersed. Benign.



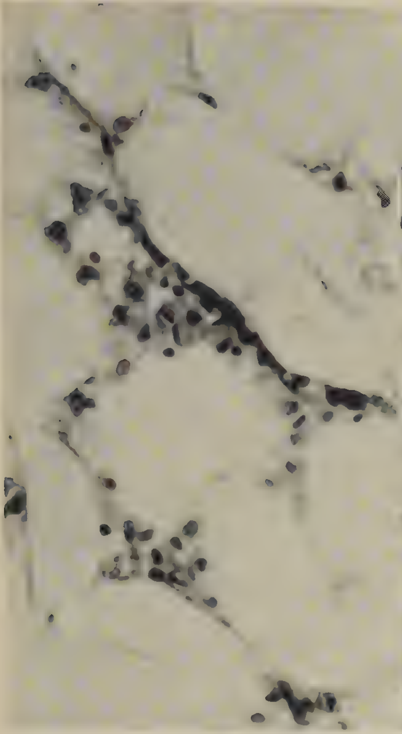
Neurilemoma. Solid Antoni type A tissue with characteristic "palisading" of nuclei. x 125.



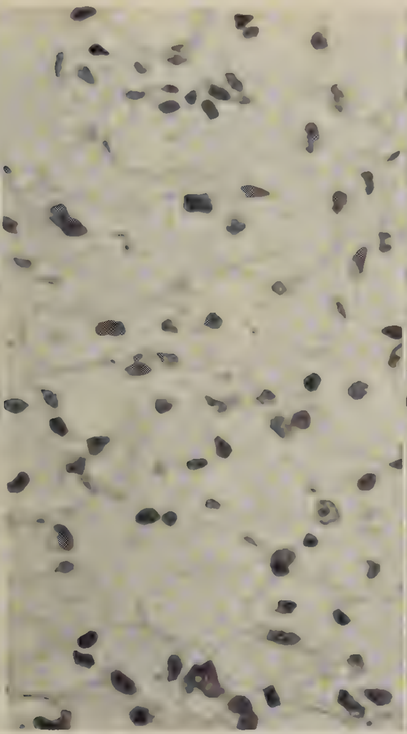
Keloid, following piercing of ear lobule. (E. R. Wert, Mobile)



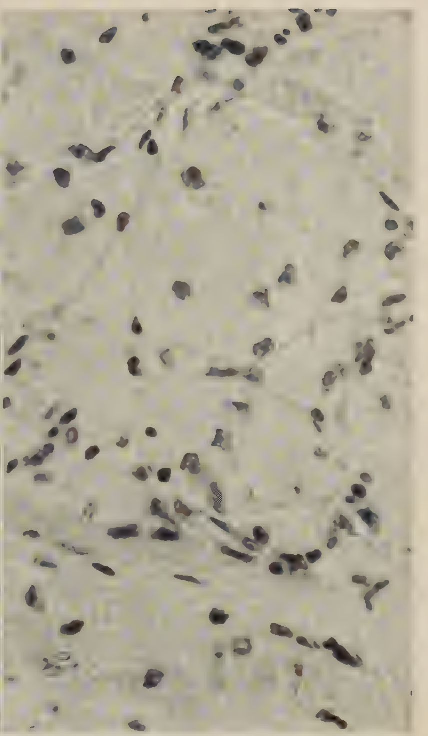
Neurilemoma, tongue. The organoid Verocay bodies are interpreted as attempts to form neural end organs. x 200.



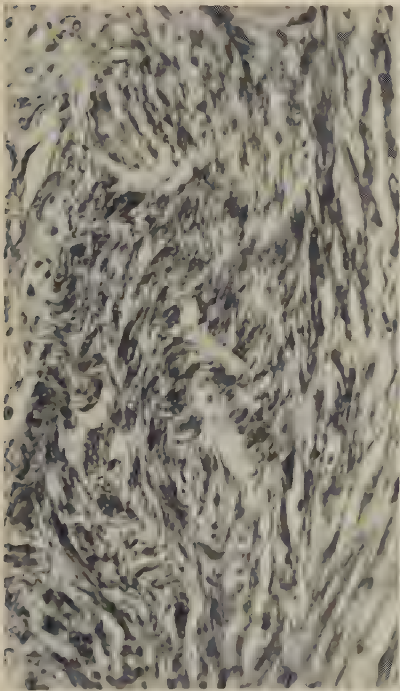
Lipoma. Lobules of mature fat cells, separated by fibrovascular septa. Cluster of small cells with incomplete fat deposition. x 500.



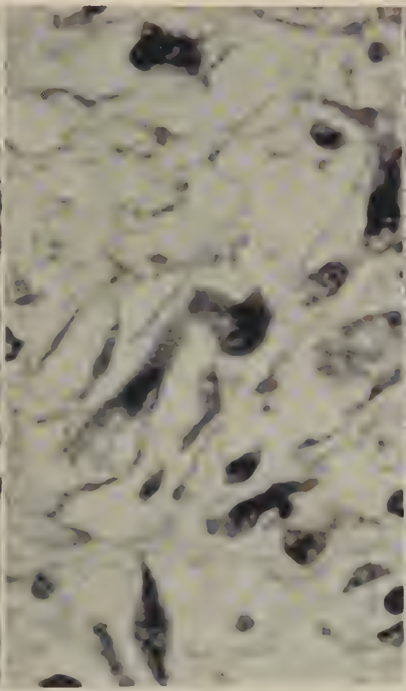
Xanthoma, larynx. Histiocytes foamy from lipid content; nuceli dark and usually centrally placed. x 700.



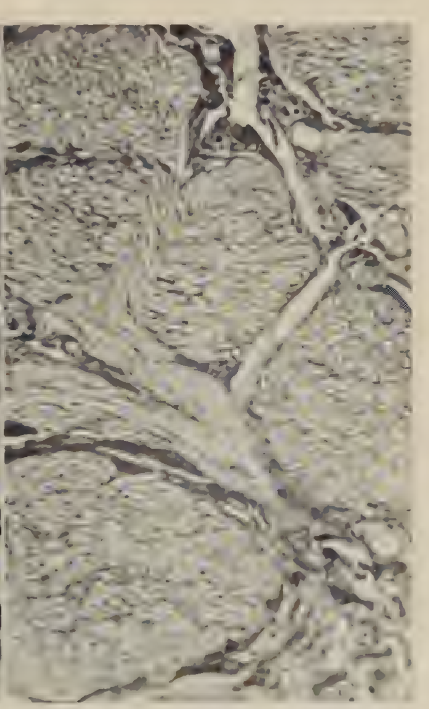
Myoblastoma, tongue. Cells resemble those of xanthoma, but are granular rather than vaculoated. x 600.



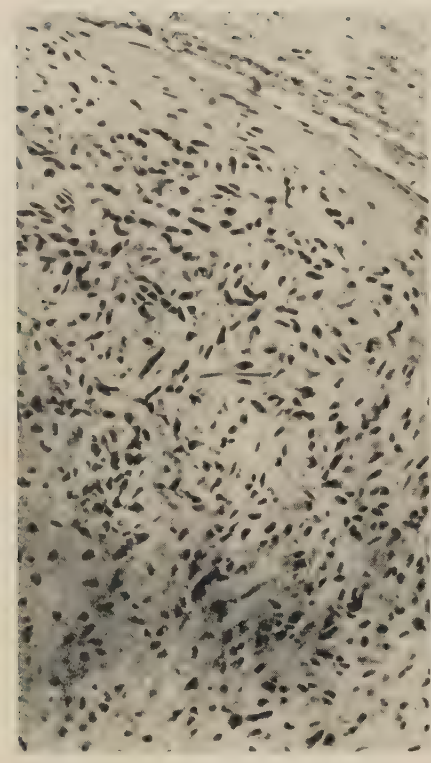
Leiomyoma, skin. Closely resembles fibroma. Cells generally richer in cytoplasm; fibers cut across look like clear cells with central nuclei. x 210.



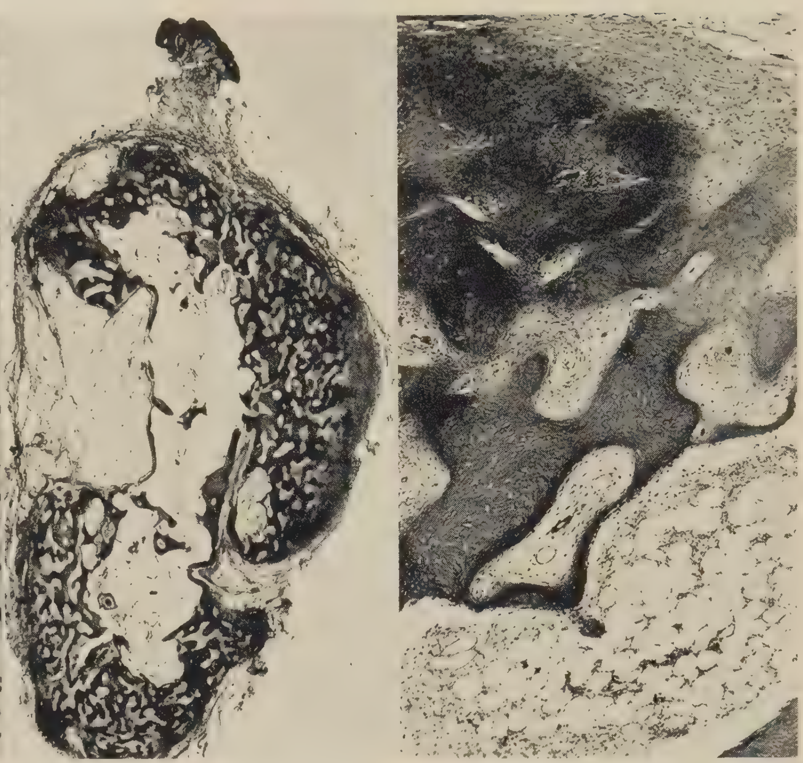
Rhabdomyosarcoma, neck. Bizarre cells; ribbony cytoplasm. Clearly defined cross-striations, such as in large cell in center, can seldom be demonstrated. x 720.



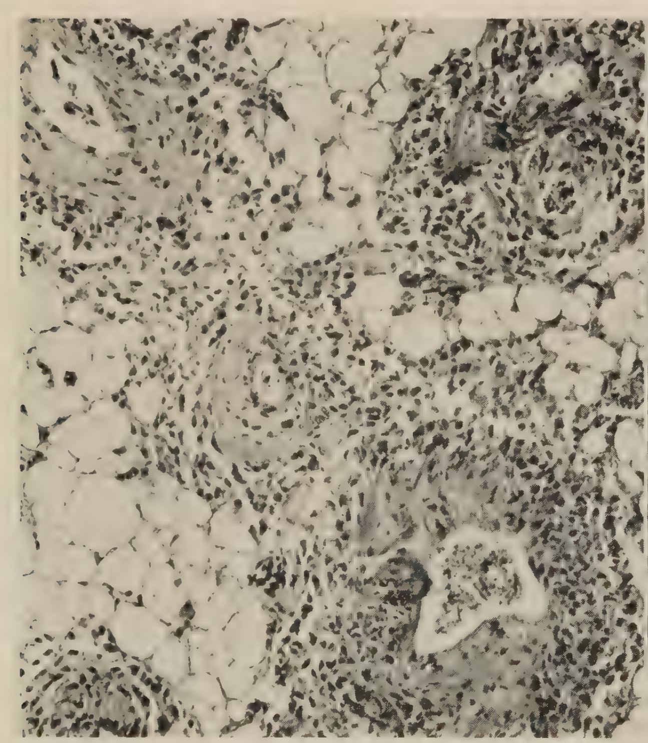
Neuroma, tongue mucosa. Bundles of medullated nerve fibers. This is an unusual site. x 125. Traumatic neuroma may follow severing of nerve.



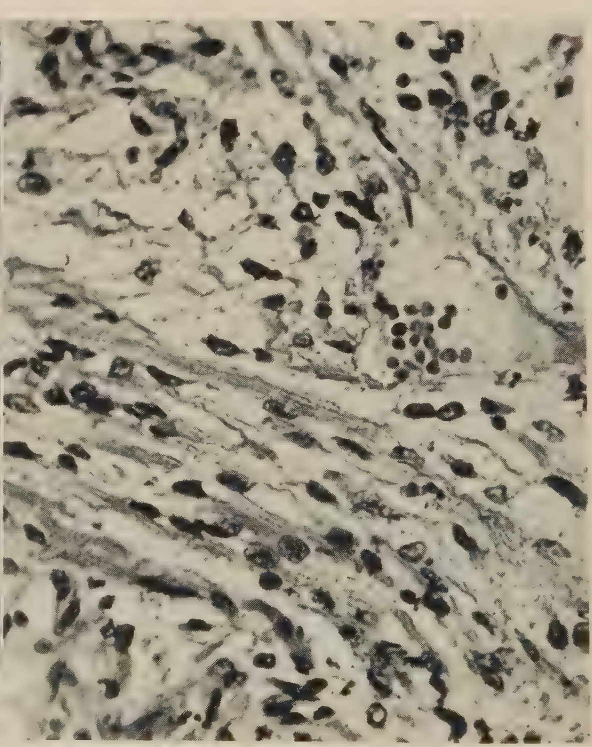
Chondroma, larynx. Cellular fibrocartilage, well circumscribed; disorderly arrangement of cells. Benign. x 150.



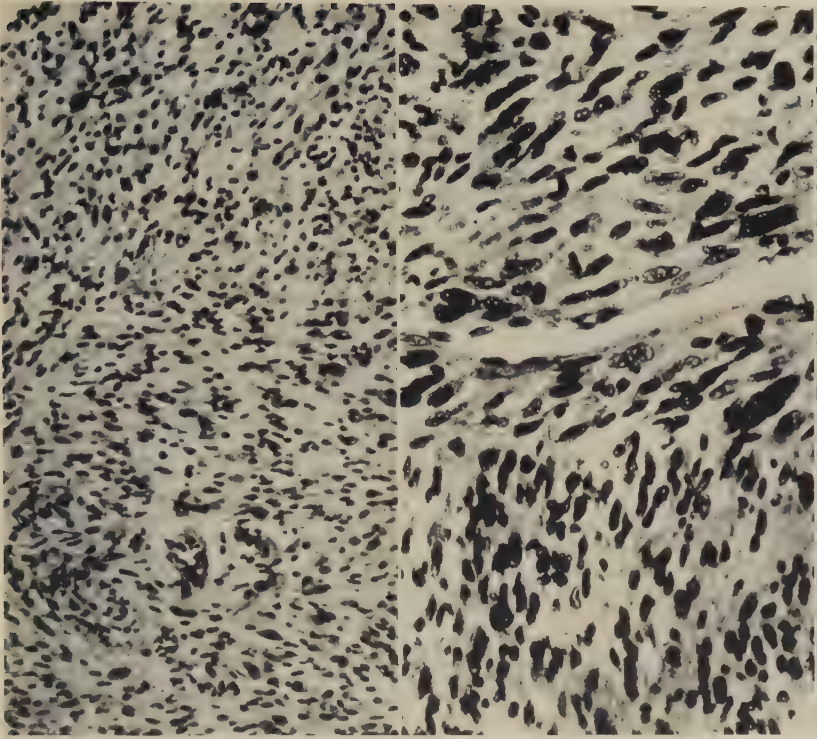
Fibro-osteoma in subcutaneous tissues of scalp behind ear. Unusual encapsulated mass of proliferating cells of possible periostial origin and well differentiated bone. Right, proliferating fibrous tissue, osteoid, and bone with hematopoietic marrow. x 48.



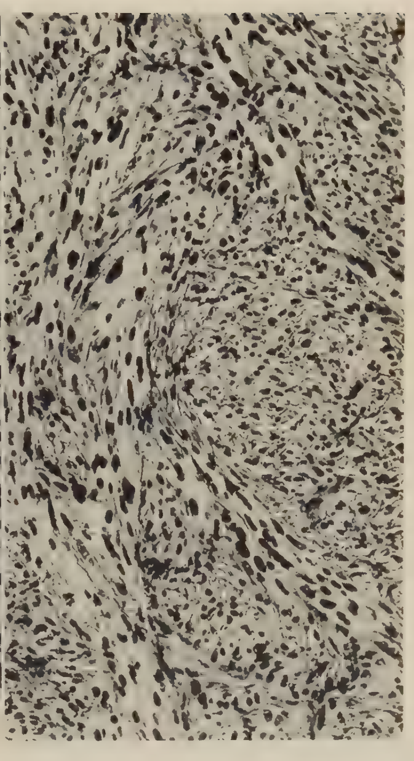
Angiomyolipoma (mesenchymoma). Mass, 4 x 2 cm., with proliferating vessels, fat, smooth muscle, and fibrous tissue as mesenchymal components. x 110.



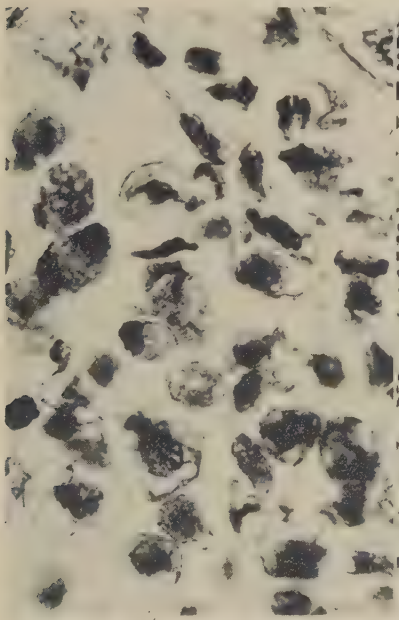
Mesenchymoma, broad ligament. The mixed mesodermal elements of this tumor included striated muscle, fibrous tissue, fat and blood vessels. x 330. Benign and malignant forms have been described.



Fibrosarcoma. Mandible of a 29 year old man. A. Cells are irregular in size, shape and arrangement; blood spaces are partially lined by tumor cells. x 135. B. Cellular detail in another tumor. x 300.

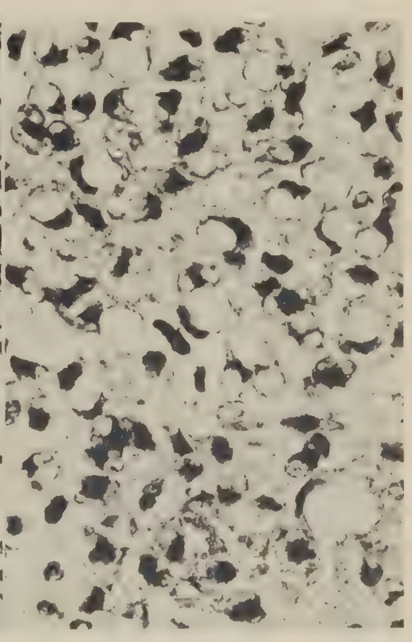


Leiomyosarcoma, bridge of nose of 52 year old man. Cells, irregular in size and shape, in interlacing bundles. x 125.

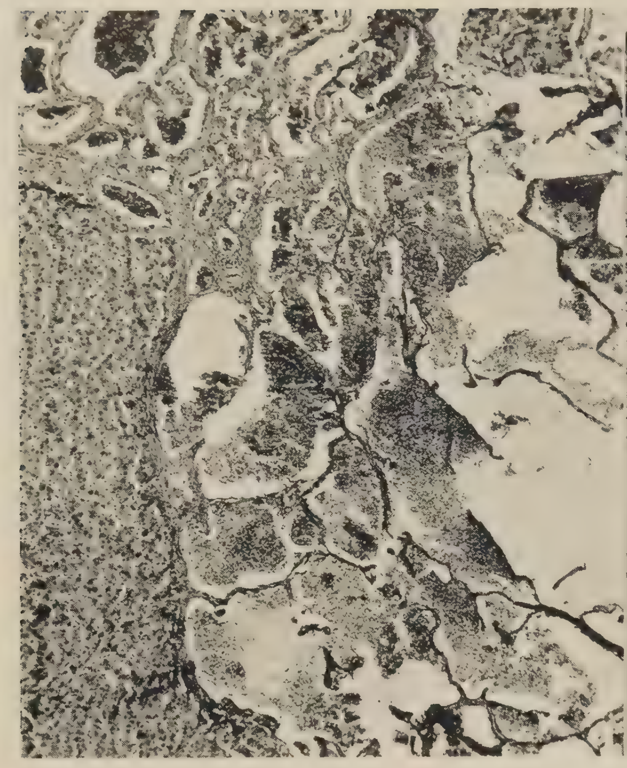


Rhabdomyosarcoma of prostate, metastatic to lung. These cells are too undifferentiated for diagnosis, which was made on other parts of tumor. x 700.

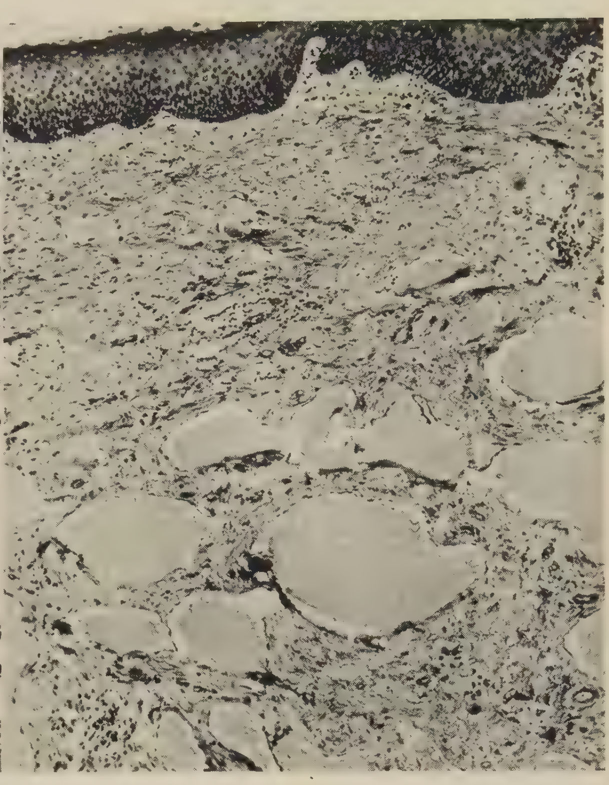
Rhabdomyosarcoma, larynx. Marked pleomorphism suggests the diagnosis. Striations are not evident. x 210.



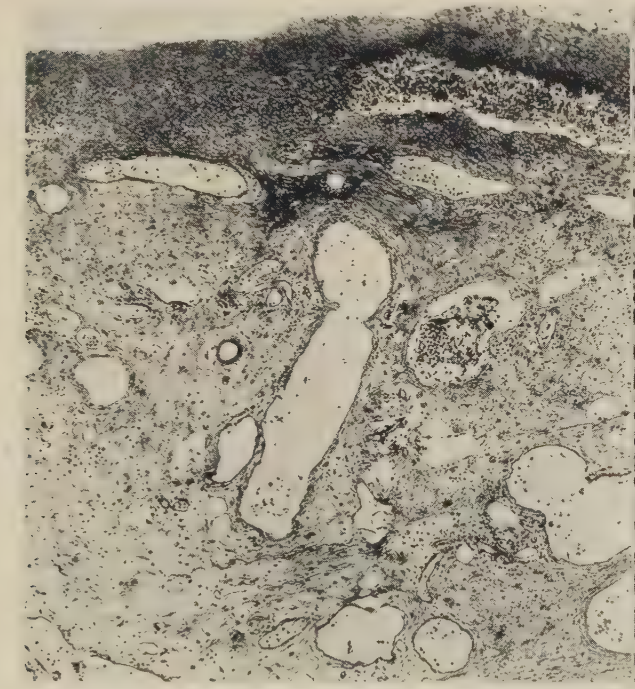
Liposarcoma, well differentiated. Many of the cells resembling signet-ring cells of carconima contain fat. Spindle-shaped or stellate cells are free of fat. x 390.



Cavernous hemangioma, liver. Large vascular spaces containing blood, lined by endothelial cells and separated by slender fibrous septae. x 48. Most benign so-called angiomas are probably hamartomas, and not true neoplasms.

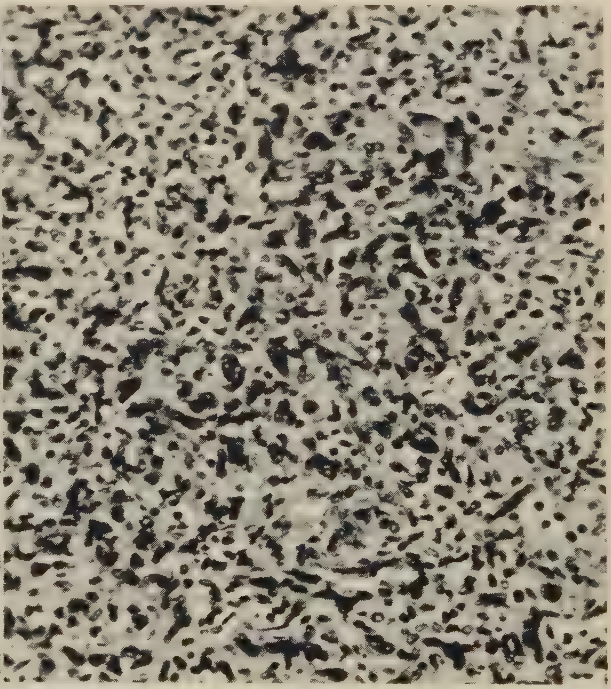


Lymphangioma, peritonsillar. Dilated endothelial lined channels containing coagulated lymph. In this area many so-called are lymphangiectases (as case above) or hamartomas. x 70.



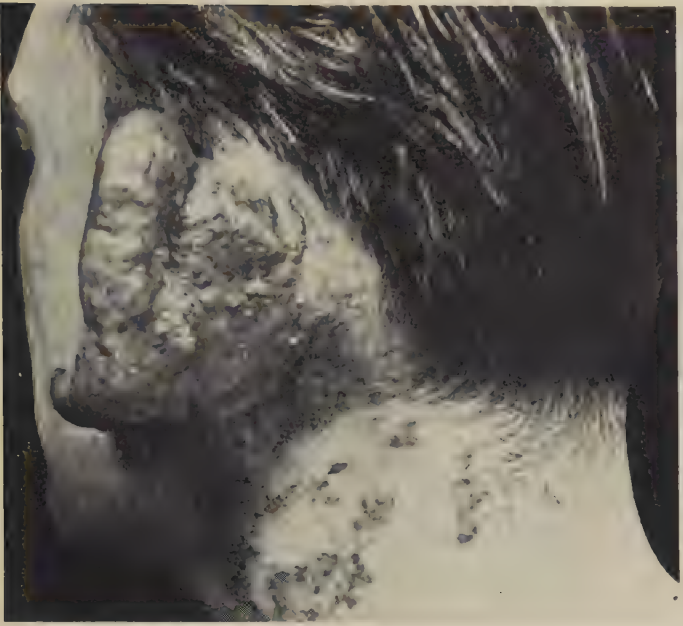
Telangiectasia, uvula, x 200, in patient who died with portal cirrhosis. Probably analagous to spider nevi of the skin and due to excess of circulating estrogens.

Any of these may be source of serious hemorrhage.

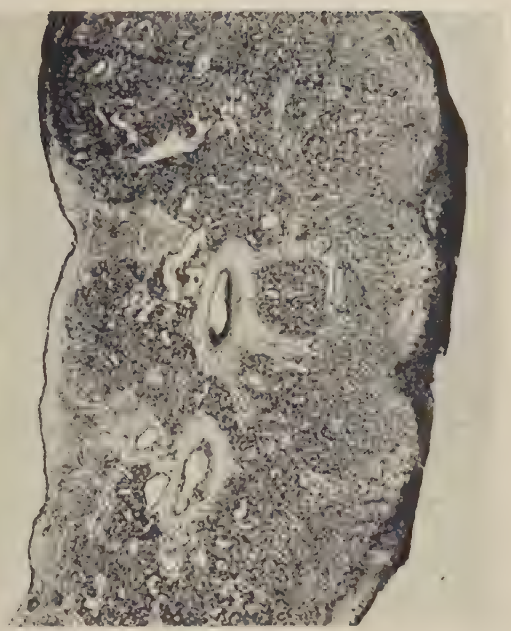


Capillary hemangioma (infantile), skin of infant. Masses of endothelial cells; numerous small capillaries with an occasional visible lumen. x 200. A congenital lesion that extends into the subcutaneous tissues in some instances.

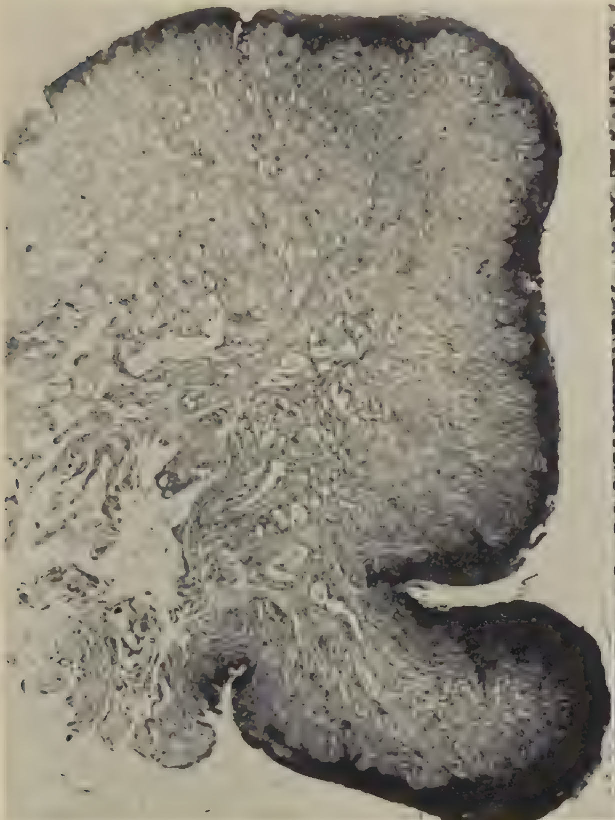
CAPILLARY HEMANGIOMA: DIFFERENTIAL DIAGNOSIS



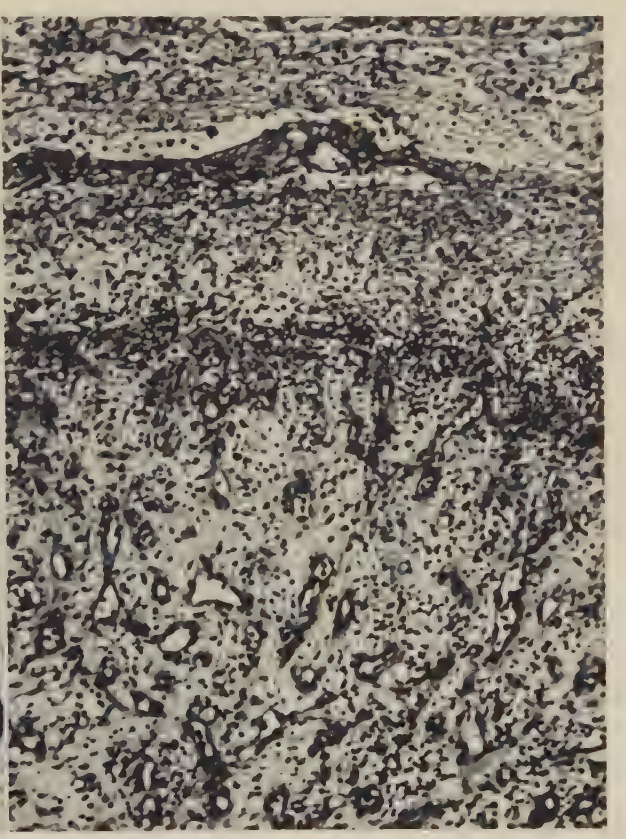
Congenital hemangioma, ear, severely traumatized while patient was a prisoner of war. Grew aggressively and ulcerated. Portions excised included reparative granulation tissue.



Granuloma pyogenicum, nasal septum. Polypoid lesion of 2 months' duration is histologically indistinguishable from capillary hemangioma with secondary ulceration. x 20.

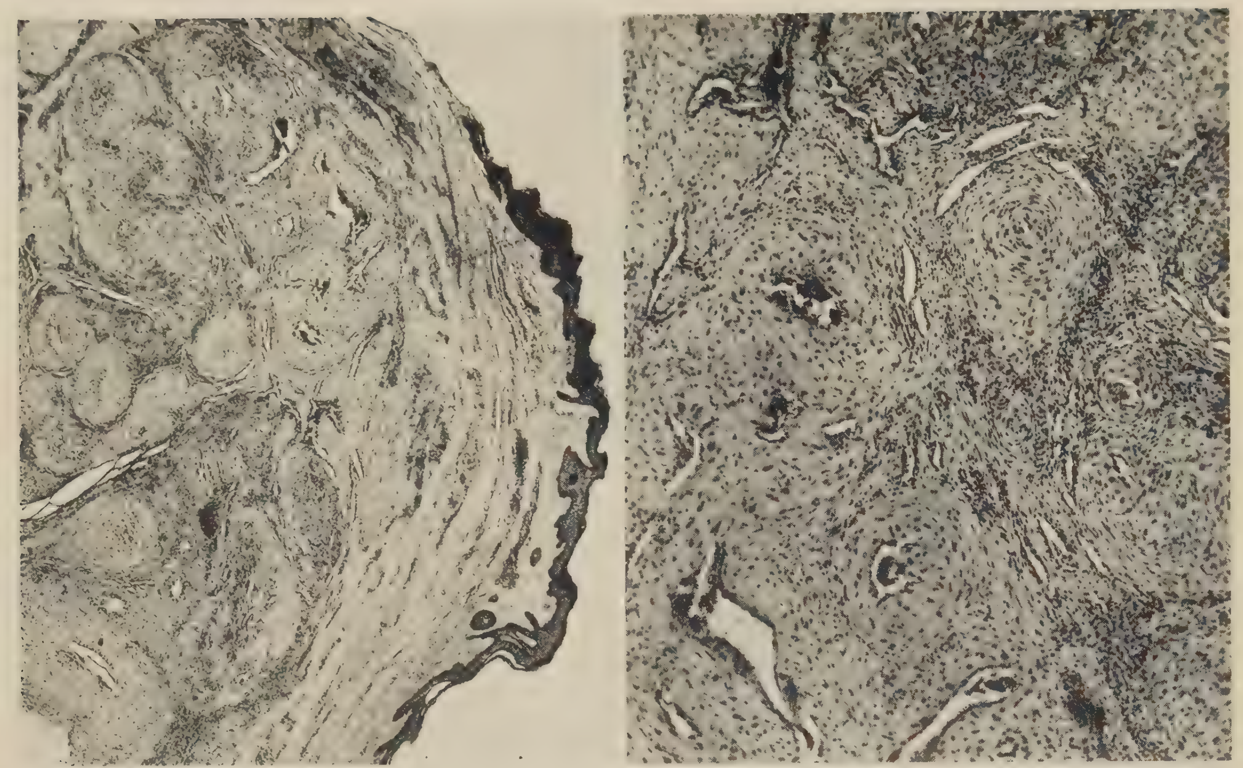


"Pregnancy tumor" (gingivitis gravidarum) which occurs in a small per cent of pregnant women. The marked vascular proliferation has microscopic features resembling true capillary hemangioma.

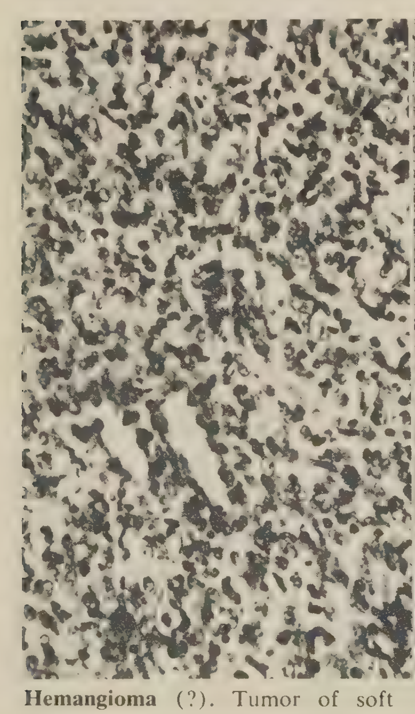


Granulation tissue, vocal cord. Post-traumatic reparative polypoid lesion; its vascular pattern may simulate the other conditions illustrated. x 114.

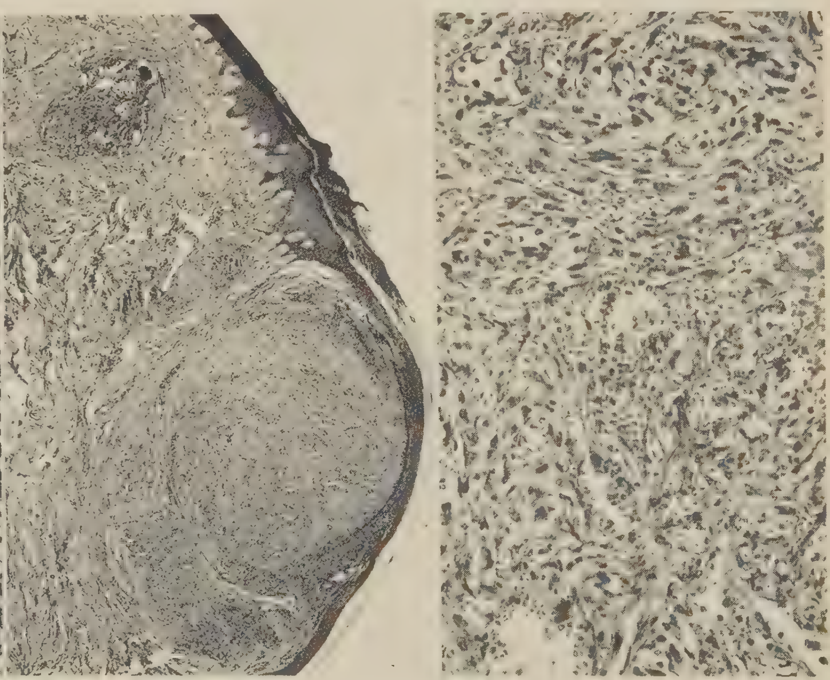
UNUSUAL TYPES



Glomangioma, ear. A painful, firm circumscribed projecting nodule. The numerous vessels have small lumens and very thick, peculiarly cellular walls with nonmyelinated nerve fibers among them. x 21. The higher magnification shows endothelial lining, and thick-walled vessels with layers of cells, which Murray and Stout have identified in tissue culture as pericytes. Benign. x 75.



Hemangioma (?). Tumor of soft tissues, preauricular, in infant. Large and infiltrating. Endothelial cells predominate. x 275.



Kaposi's (multiple ideopathic hemorrhagic) sarcoma. Two skin nodules in case with, as yet, no visceral involvement. x 47. Vascular area with blood-filled spaces, hemosiderin deposition and a typical proliferating cells. x 235. Considered essentially an angiosarcoma. Some believe there may be a significant relationship to malignant lymphoma because of their concurrent association in a number of cases.

CHAPTER 9

DERMATOSES

In addition to the tumors that arise in the skin, mucosae, and their appendages, there are other diseases of these structures with which the otolaryngologist must be familiar. By way of orientation in the histology of these and as an introduction to the language of the dermatologist a few definitions are necessary.

The BASAL LAYER of the surface epithelium is made up of palisaded cells containing more or less melanin pigment. The rete pegs or ridges are produced by the papillations of the superficial portion of the true skin or dermis. As mentioned in the discussion of basal cell tumors, it has been proposed that there are two potentially, if not morphologically different basal cells, one forming the covering squamous prickle cell layer of the STRATUM MALPIGHII and the other destined to form the skin appendages—the glands of various types and the pilosebaceous elements.

As the cells of the prickle layer mature and become the upper layers, they begin to show the peculiar senescent change of **keratosis.** This consists of an elongation of the cell, the loss of prickles, and the accumulation of dark granules of keratohyalin in the cytoplasm. They then constitute the GRANULAR LAYER. The final stage is loss of cell nucleus and granules, leaving a thin flake of keratin on the skin surface. The process of keratinization is normally not so sharply defined in mucosal squamous epithelium.

Pathologic changes may affect any or all of these stages of maturation. The simplest is hyperplasia with great thickening of the prickle-cell layer called **acanthosis.** In simple acanthosis there is hyperplasia of only the prickle-cell layer in which the individual cells are normal and the processes of maturation and keratinization are not interrupted.

Pseudoepitheliomatous (pseudocarcinomatous) hyperplasia is a special type of acanthosis frequently seen as a response to chronic ulcerative conditions of the skin and mucosa. Examples of it will be seen in several sections of the Atlas. There is great exaggeration of the rete pegs, which extend deep into the underlying tissue. The cells include mitotic figures, and the basal cells have a young appearance and have lost much of their polarity. The resulting picture is difficult to differentiate from actual malignancy and is not infrequently so interpreted by the pathologist.

Hyperkeratosis is an increase in the keratin layer with or without acanthosis. Pachydermia of the larynx and hyperkeratosis of the tonsils are clinical forms that are of interest to the otolaryngologist. It is seen more specifically in verrucous lesions and in traumatic hyperplasia such as callus and corns. An exaggerated clinical form sometimes seen on the face is the CORNU CUTANEUM. Another clinical type is the HAIRY TONGUE that results in great elongation of the filiform papillae.

Parakeratosis results when the process of keratinization is altered so that the granular layer is lost and the cells on the surface retain their elongated pyknotic nuclei. It is a feature of several specific dermatoses, for example, psoriasis and the more active areas of leukoplakia.

Dyskeratosis.—The process of keratinization may become so disordered that mature cells are found even in the basal layer. Keratinization may take place in the prickle-cell layer, or there may be apparent direct transition from basal cells to fully keratinized cells. This series of pathologic changes is called dyskeratosis. It is possible to divide the various types of dyskeratoses into benign and malignant. Long clinical experience has shown that certain types never undergo carcinomatous transformation but that others do so in varying percentage.

Two only of the BENIGN DYSKERATOSES need to be presented here. SEBORRHEIC KERATOSIS (VERRUCA SENILIS) is one of the senile changes of the skin and consists clinically of a warty, black, greasy mass that projects above the skin surface. It is most common on the face, back, and chest, interestingly enough, in about the same distribution as the basal cell tumors.

Microscopically, it is made up of a mass of exaggerated and fused rete pegs in which the cells have retained their basal character. They are usually heavily pigmented with melanin. In spite of the absence or greatly reduced number of mature cells, there is an excess of keratin on the surface and in the crypts. One of the histologic characteristics is the keratin cysts in the deep portions resulting from transverse section of the crypts.

MOLLUSCUM CONTAGIOSUM is a mildly contagious viral disease. It is characterized clinically as multiple, but at times single, small nodules which are elevated above the skin surface, with a crater-like center and a sago-like appearance. They occur most commonly on the face, particularly on the eyelids and forehead.

Histologically, there is a sharply outlined cup-shaped mass of epithelium with a prominent basal layer which changes abruptly into squamous cells. In those toward the surface, dark granules of keratohyalin and eosinophilic droplets appear. These seem to agglutinate and form round bodies which eventually occupy practically the entire cell. These are the molluscum bodies. There is disagreement as to whether these are inclusion bodies and evidence of a viral etiology or simply the result of the peculiar cell dyskeratosis. They are probably a combination of both.

Other types of benign keratosis are Darier's disease and acanthosis nigricans that do not concern us here.

Malignant dyskeratoses are of much more importance. The first and commonest type is called LEUKOPLAKIA when the lesion occurs in mucosae and SENILE KERATOSIS when it occurs in the skin. On the mucous membrane this form of dyskeratosis is seen as flat areas of white thickening which most commonly occur on the vermilion border of the lower lip, but also on the buccal mucosa, the tongue, larynx, faucial tonsils, vestibule of the nose, in fact, in any situation where squamous mucosa exists normally or as a result of metaplasia. It may cover several centimeters of surface. This flat type presents little clinical evidence of inflammation. It may remain dormant for years or, especially on the lips or the tongue, may develop fissures or areas of ulceration. Such activity must be interpreted as indicating malignancy. The lesions on the buccal mucosa are characteristically innocuous and generally should not be disturbed.

The other form is a local piling up of epithelium which projects above the surface as a wart-like lesion, sometimes with a larger surrounding zone of inflammation. This is the verrucous form and is most common on the lip, the eyelid, in the nares, on the ears and backs of the hands, all places that are exposed to sunlight. It is the form most commonly taken by senile keratosis and which usually eventuates in frank squamous cell carcinoma.

Microscopically, in both leukoplakia and senile keratosis there is more or less acanthosis with hyperplasia of the rete pegs which may be irregular in shape and penetrate deeper into the dermis than do the pegs of the adjacent normal epithelium. Dyskeratosis begins in the basal layer as evidenced by the presence of rounded cells with prominent nuclei that may replace long stretches of the normal basal type of cell. Buds of these cells may extend beyond the basement membrane. The dyskeratosis extends through the prickle-cell layer, where the cells are of irregular size and shape, with mitotic figures that may be atypical, and show evidence of premature keratinization. The granular layer may be entirely absent and the surface layer parakeratotic. In the verrucous formations the surface is thrown up into projections that may have vascular fibrotic stalks usually covered by a thick layer of epithelium with keratosis that varies in amount and extent. There is always chronic inflammatory reaction in the contiguous dermis and this may invade the basal layer and further blur its outline.

Some pathologists, particularly among the dermatologists, insist on calling dyskeratosis of this type CARCINOMA IN SITU. This practice may be confusing and clinically inaccurate because, despite the abnormal cells, the lesion may exist for years before there is frank invasion. The borderline between leukoplakia and squamous cell carcinoma is certainly not sharply drawn, and for practical purposes the diagnosis of carcinoma should not be made until there is frank invasion of the dermis by groups and strands of neoplastic epithelium that have severed connections with the basal layer of the epidermis.

Bowen's disease is a clinical entity which consists of single or multiple clusters of papules that may be verrucous or crusted. It occurs occasionally on the face and the body, but most commonly on the lower extremities. This is a very chronic, slowly-progressing disease, and although carcinoma has been known to develop in these lesions, it is uncommon.

Histologically, it somewhat resembles the dyskeratosis of leukoplakia except that there is not the irregularity in the basal cell layer and the dyskeratosis involves individual cells scattered through the malpighian layer. These cells may be very large giant epithelial cells and multinucleated epithelial giant cells, or they may be smaller, with hyperchromatic nuclei about which there is a clear zone. The latter are indistinguishable individually from the abnormal cell seen in Paget's disease of the nipple. These cells may be grouped in clusters of three or more. Mitotic figures are not as common as in leukoplakia. The surface may be verrucous or flat, but a prominent granular layer and hyperkeratosis are constant features.

The **Bowen type of dyskeratosis** has been reported in the mucous membranes of the conjunctiva, the larynx, epithelial papillomas of the nasal cavity and the cervix, as well as in the skin. There is a question as to whether such lesions should be included under the clinical term Bowen's disease. We prefer to call it the Bowen type of dyskeratosis, or bowenoid. Involvement of the mucosae in classic Bowen's disease, however, has been reported.

The malignant dyskeratosis which results from irradiation has been described in the chapter on ionizing radiations. A very similar picture may develop in arsenical intoxication, particularly with the inorganic forms. As in response to irradiation, there may be an acute fulminant reaction from therapeutic arsenic, particularly the organic compounds such as salvarsan, or a more delayed and chronic arsenical dermatitis with pigmentation and papillary scaling lesions as was seen following the prolonged use of atabrine. However, the precancerous form is, as in irradiation injury, a keratosis. These lesions are more characteristically located on the palm of the hands than on the dorsum where lesions of senile keratosis and irradiation are found.

The other malignant dyskeratoses are Paget's disease of the nipple, erythroplasia of the glans penis, and xeroderma pigmentosum. With the exception of the last they are not pertinent to this Atlas.

Xeroderma pigmentosum does affect the face because it is related to some extent to hypersensitivity to light. It begins in childhood and in the early stages may be mistaken for freckles. Because of this photosensitivity the disease is characterized by exacerbations in summer. At times it involves the whole body in a scaly, papillary, ulcerating process with multiple keratoses. It is in these keratoses that carcinoma eventually develops. This is one of the dermatoses that shows the paradox of atrophy of the prickle layer but an excess of keratin.

INFLAMMATORY DERMATOSES

Lichen planus is seen usually in adult life. The cause is not known. It is characterized clinically by glistening, brownish or reddish-brown, flat papules, discrete in the early stages, about the size of a pinhead, and tending to be angular in shape. The surface has a characteristic shiny appearance. Later these individual lesions coalesce and form larger plaques or thin, lacy strands. The surface usually becomes dark with age and finally scaly. The oral mucosa may be involved along with the skin or it can be involved alone. Here lichen planus occurs most commonly on the buccal surface and is present as irregular, white, smooth, slightly elevated patches, or in the more lacy pattern. It can simulate leukoplakia very closely.

The histologic picture is usually diagnostic. It consists of moderate acanthosis, a sawtooth-like hyperplasia of the rete pegs, an increase in the granular layer of the epidermis, and moderate hyperkeratosis. An exudate of small mononuclear cells is intimately associated with the basal layer of the epithelium but is sharply demarcated from the deeper layers of the dermis. Small areas of liquefaction necrosis occur in the basal layer of the epithelium. In the older lesions the melanin pigment in the basal layer is increased and some is distributed through the dermis by means of phagocytes.

Dermatitis medicamentosa.—The antibiotics, many drugs, and various preparations including cortisone induce in the skin practically the entire gamut of reactions of which it is capable, from a mild local erythema to severe generalized exfoliative dermatitis and even gangrene. With few exceptions these reactions are not specific to any particular drug, but the degree of response is largely determined by individual sensitivity. Arsenic, as mentioned under the malignant dyskeratoses, may cause a generalized acute reaction closely associated with the administration of an organic form of the drug; and a chronic type, at times with keratotic precancerous lesions, usually following prolonged exposure to inorganic arsenic. Illustrations of the late stage of atrophy and pigmentation in the therapeutic type and also of the keratotic reaction are included in the following plates.

The prolonged use of iodides and especially of bromides usually results in recognizable lesions. They are generally localized, of acne or carbuncle type, and commonly occur about the face. Less common but more typical are the large, hyperkeratotic, ulcerating sores, usually on the legs. The pseudocarcinomatous hyperplasia of the epidermis is a histologic characteristic.

Seborrheic dermatitis, particularly troublesome in the ear, is described in the section on that organ. An illustration, however, is included in the following plates.

Vesiculation is a feature of a number of conditions pertinent to this Atlas. The dermatologist recognizes several types of vesicles in addition to those distinguished morphologically by their size—vesicle, bleb, and bulla. Among these are the vesicles that develop as a result of edema between and in the cells of the epidermis, as in eczema; those that result from a peculiar hydropic degeneration of cells, called ballooning, as seen in the viral diseases (herpes zoster and smallpox, for examples), and the so-called pressure vesicles and bullae due to local accumulation of fluid rather than to degeneration of the epithelial cells, as in pemphigus.

Impetigo contagiosa is an acute, contagious inflammatory disease particularly common in children. It occurs most frequently on the face and can be especially troublesome about the nares. It is characterized clinically by the presence of superficial, lightly attached, thin crusts, which, when removed, leave a slightly raw surface. The lesions begin as small red patches or vesicles which rapidly become pustular. The crusts noted clinically form on these pustules.

Histologically, the lesion is a superficial vesiculation of the epidermis which usually involves only the stratum corneum. The pustular vesicle contains great numbers of polymorphonuclear leukocytes. There is some dilatation of the small vessels in the papillary layer of the dermis but little other inflammatory reaction.

Herpes simplex (fever blister, cold sore), while usually occurring about the lips and nares, does involve the mucosa and may develop anywhere in the upper respiratory tract, including the larynx. Vesiculation is not so much a feature in the mucosal lesions, which are generally points of superficial ulceration.

The vesicles are very small and develop from coagulation necrosis and by ballooning degeneration of the epithelial cells. Acidophilic nuclear inclusions of Lipschütz can be seen in the involved epithelial cells.

Herpes zoster (shingles) is a more complex disease in that the posterior roots of the spinal nerves are affected as well as the skin. The distribution of the dermal lesions is largely dependent on the nerve root affected. The ophthalmic form of herpes zoster is particularly serious, for the peripheral vesiculations may involve the conjunctiva and cornea. Because of the nerve involvement neuralgic pain is a prominent clinical symptom.

The vesicles of zoster are deeper in the epidermis than those of the simplex form and they show the typical ballooning degeneration of the epithelium. There is also greater reaction in the dermis—vascular dilatation, edema and exudate. Inclusion bodies are present in the nuclei of the epithelial cells as in herpes simplex.

Sycosis vulgaris is a pyogenic disease of the hairy parts of the face of the male. Unlike impetigo, it is a chronic refractory disease of the hair follicles characterized clinically by papules and pustules in which hairs can usually be detected. A large portion of the face is often involved. Affection of the upper lip is a not uncommon complication of persistent purulent rhinitis. A variety of the pyogenic bacteria are generally concerned.

Histologically, the hair follicles are the site of an indolent, suppurative, inflammatory reaction that extends into the surrounding dermis. The orifices of the hair follicles are often plugged with exudate, bacteria, and keratinous debris. The epithelium of the hair follicles is usually infiltrated by the exudate and the hair follicles may be destroyed. Healing of such areas is chiefly by scar formation, and the chronicity of the process is indicated by some proliferation of fibroblasts in the dermis.

Tuberculosis involves the skin in a variety of clinical forms. We need mention only a few of them. The most important is LUPUS VULGARIS. This entity has no relationship whatever to lupus erythematosus and the confusion of terms results from the early notion that the latter was a form of cutaneous tuberculosis. Lupus vulgaris is the commonest form of tuberculosis of the skin, but it is not so frequently seen in this country as in Europe. It usually occurs on the face, particularly about the nose from which it spreads to the cheeks, but it may also originate on the neck or about the ears. The process begins as small, soft, reddish or yellowish papules which coalesce. The eventual result is a large verrucous process with caseation and scarring. With the peripheral spread of the process there is healing and scarring in the center.

Histologically, the epidermis shows more or less acanthosis and hyperkeratosis and occasional ulceration. The dermis is infiltrated with chronic exudate, and diagnostically typical tubercles also form, usually in the upper dermis, but occasionally the deeper portions are involved. Tubercle bacilli can be demonstrated in these granulomas but there is not the degree of caseation here that is seen in active tuberculosis elsewhere.

Tuberculosis of the mucosa of the lips and mouth is called TUBERCULOSIS CUTIS ORIFICIALIS. It manifests itself as relatively superficial ulcers, usually discrete, with fairly well circumscribed borders. This condition is very indolent clinically. The lesions are usually a complication of active pulmonary tuberculosis and occur particularly about the lips and on the tongue. Tuberculosis of the buccal mucosa may take a more verrucous form when it must be differentiated from aphthous ulcers and carcinoma. This can be done by biopsy or by the demonstration of tubercle bacilli in scrapings.

Lupus erythematosus is usually a chronic but sometimes acute disease of the skin, most commonly of the face, characteristically including the bridge of the nose and the malar eminences in a butterfly pattern. It may, however, involve any portion of the face, neck, or ears as more circumscribed lesions. These are characterized by a central, relatively smooth, somewhat atrophic area bordered by a slightly papillary and scaly process showing a varying amount of erythema. On closer examination, especially with a loupe, the enlarged hyperkeratotic hair follicles can be distinguished. The lesions extend peripherally.

The disease occurs most commonly in the cooler climates and it affects young adult women more frequently than men.

Clinically there are two main types—the CHRONIC DISCOID which remains localized to the skin, and the DISSEMINATE in which there is a systemic involvement of collagenous tissue, including the heart valves and endocardium, the kidney, spleen, and blood vessels. The second form is fatal. The differentiation between the two forms is not evident in the skin lesions either clinically or histologically.

The histologic picture is usually diagnostic. The epidermis shows varying areas of atrophy and acanthosis; the hair follicles are blocked with keratin; the basal layer of the hair-shaft epithelium shows foci of liquefaction necrosis, and the vessels in the upper portion of the dermis are dilated, accounting for the clinical erythema. Degeneration of the elastic and collagenous elements of the dermis is evidenced by blue-stained granular or hyaline masses in the upper dermis. There is considerable chronic inflammatory reaction, rather nodular in distribution and usually in close association with the hair follicles. There are, however, no tubercles.

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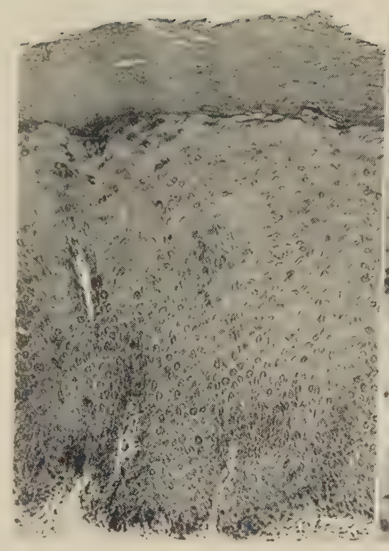
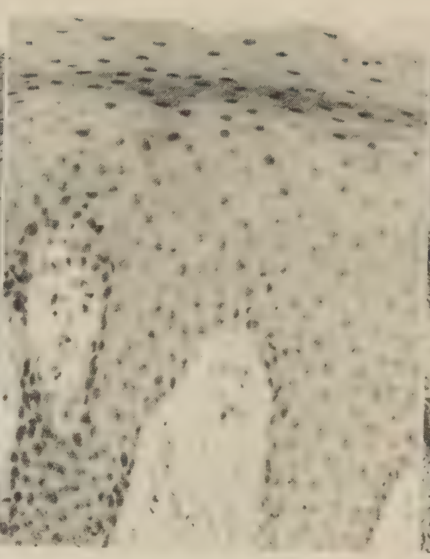
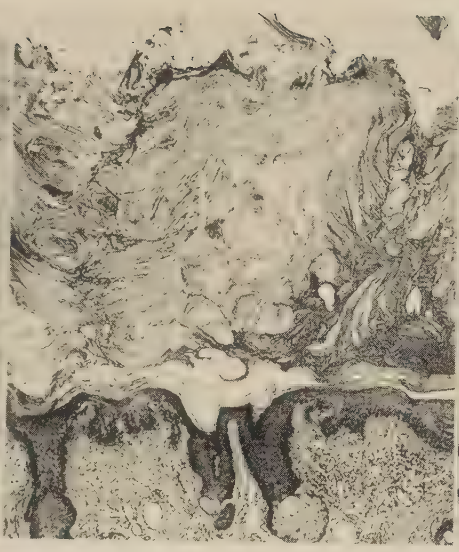
HISTOLOGIC EPITHELIAL CHANGES



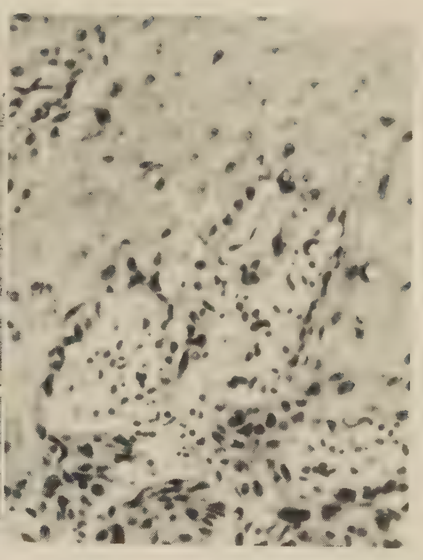
Acanthosis: increased thickness of the prickle-cell (malpighian) layer. Hyperkeratosis frequently present, as above.



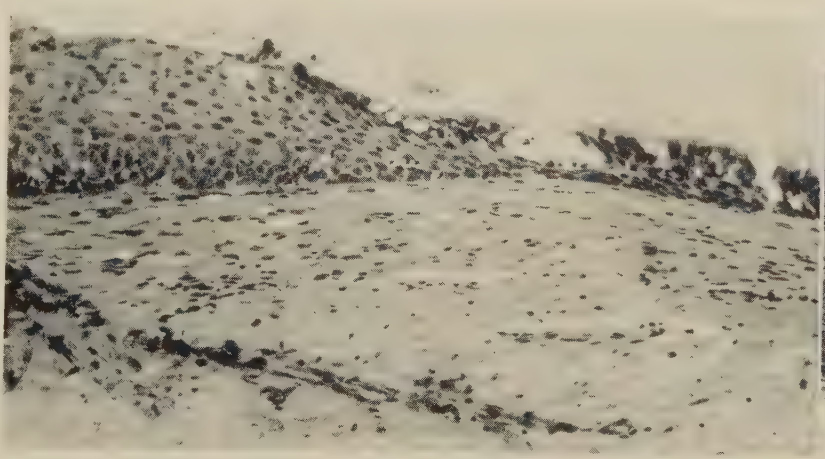
Parakeratosis: retention of nuclei in the stratum corneum. The granular layer is commonly absent or inconspicuous.



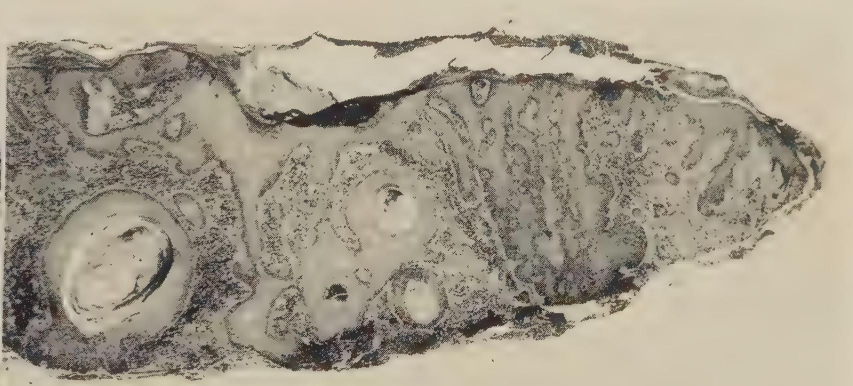
Hyperkeratosis: increased thickness of the keratin layer, the stratum corneum. Usually associated with a thickened granular layer.



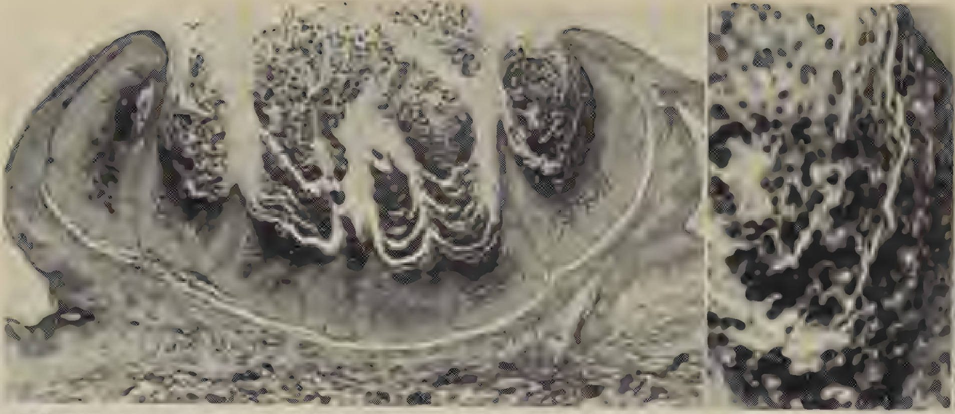
Dyskeratosis: abnormalities in epidermal cells due to faulty maturation, such as premature keratinization, etc. Benign and malignant types.



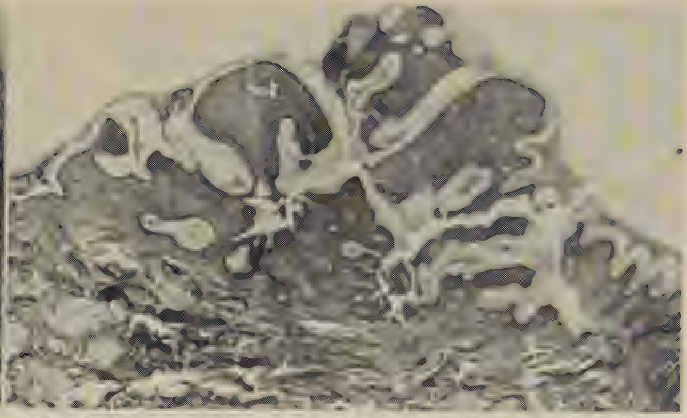
Metaplasia: change in cells of a tissue to a type not normally present. Metaplasia of ciliated respiratory epithelium of frontal sinus (right) to stratified squamous epithelium (left) as result of chronic inflammation. x 320.



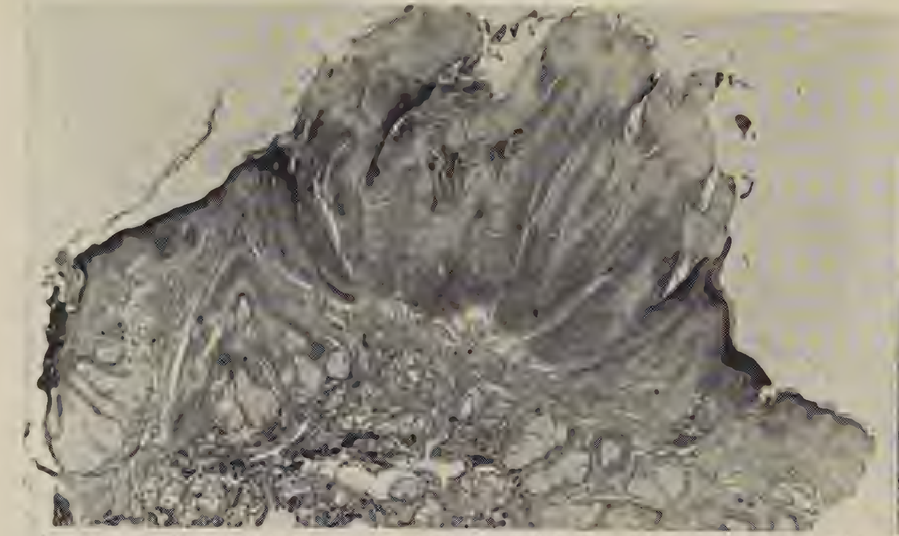
Pseudoepitheliomatous hyperplasia: nonmalignant proliferation with downgrowth (acanthosis) and often fusion of rete pegs, which may simulate carcinoma. Section from sinus tract into frontal sinus. x 30.



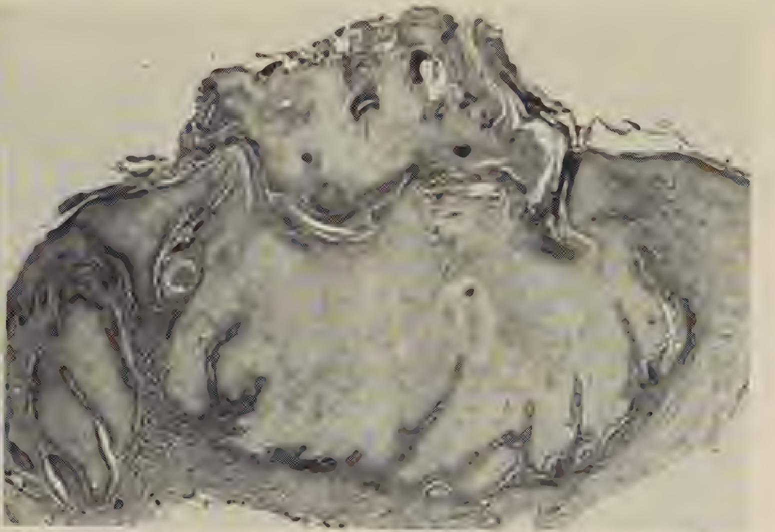
Molluscum contagiosum. Mildly contagious, autoinoculable virus disease. Sharply circumscribed, elevated, oval or round, smoothly lobulated lesion with extensively keratinized central core communicating with center of each lobule. Numerous "molluscum bodies" in upper epidermis and central keratin mass. These are cells with nuclei displaced to one side by the homogeneous eosinophilic cytoplasmic inclusion bodies, in which elementary bodies have been demonstrated with vital stains. x 25. The intensely eosinophilic "molluscum bodies" appear black. x 105



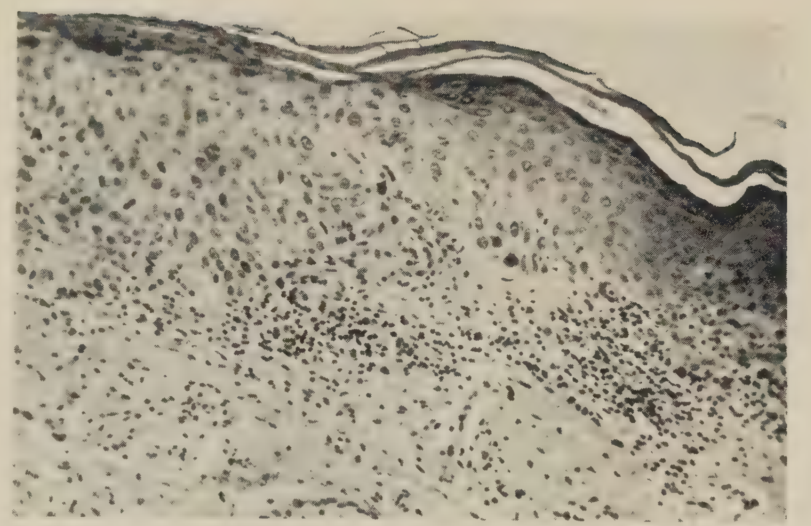
Seborrheic keratosis (verruca senilis; pigmented inverted papilloma [Willis]). Circumscribed, elevated lesion, in this case, verrucous. Characteristic winding acanthosis which may enclose portions of dermal papillae. That the keratin cysts are due to the downgrowth and invagination of the surface epidermis is well shown in this case. Lower epidermal layers heavily pigmented; no dermal inflammation. x 20. Classified as benign epidermal neoplasm.



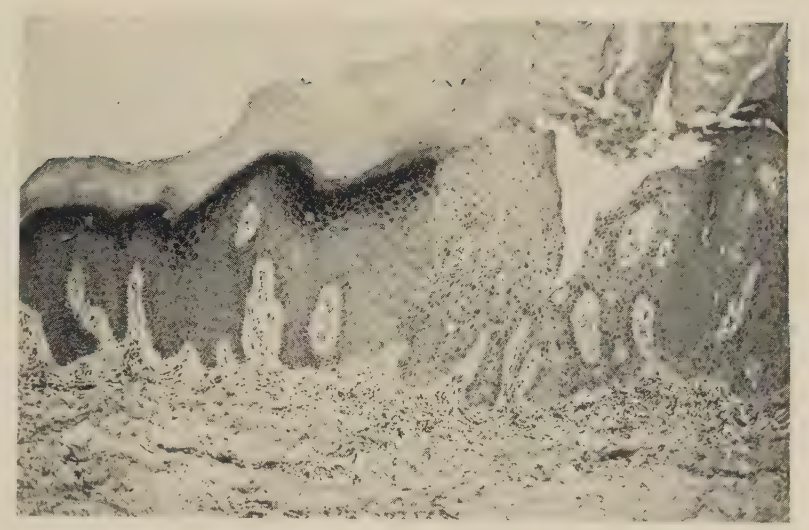
Verruca vulgaris (wart), lip. Circumscribed elevated lesion with horny surface. Papillary hyperplasia of epithelium; marked acanthosis and hyperkeratosis with characteristic intermittent parakeratoses. No inflammatory exudate in dermis at base. x 25. Presence of inclusion bodies in early lesions, autoinoculability, and experimental evidence indicate a viral etiology.



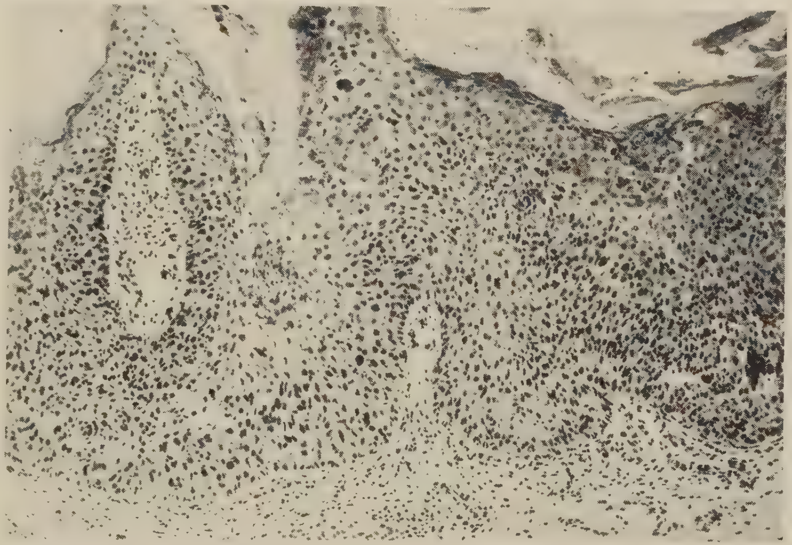
Leukoplakia, verrucous type, lip. Superficially resembles verruca vulgaris with marked acanthosis and hyperkeratosis. Numerous mitoses and dyskeratosis in local and prickle cell layers. Dense inflammatory infiltrate in adjacent corium is predominantly lymphocytic. x 15.



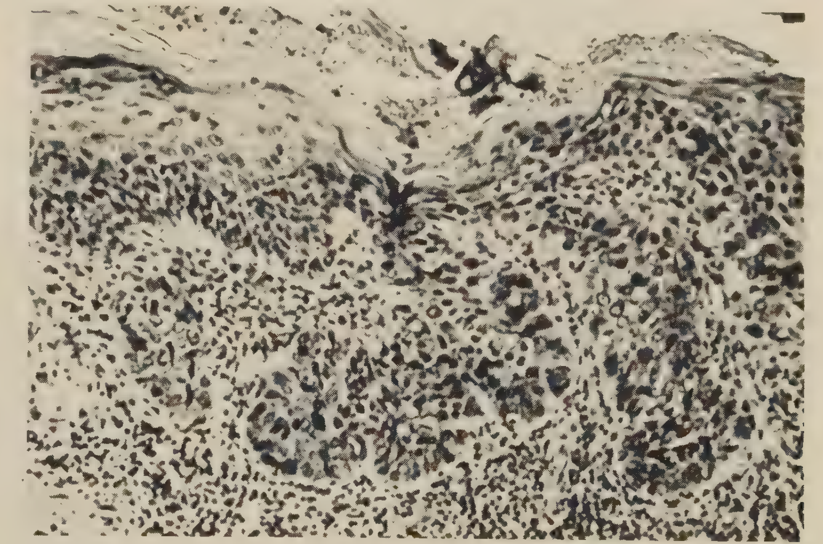
Leukoplakia. Dyskeratotic lesion of mucous membrane. Hyperchromatic atypical cells; mitoses; and loss of polarity. Parakeratosis, upper left; keratosis, upper right. x150.



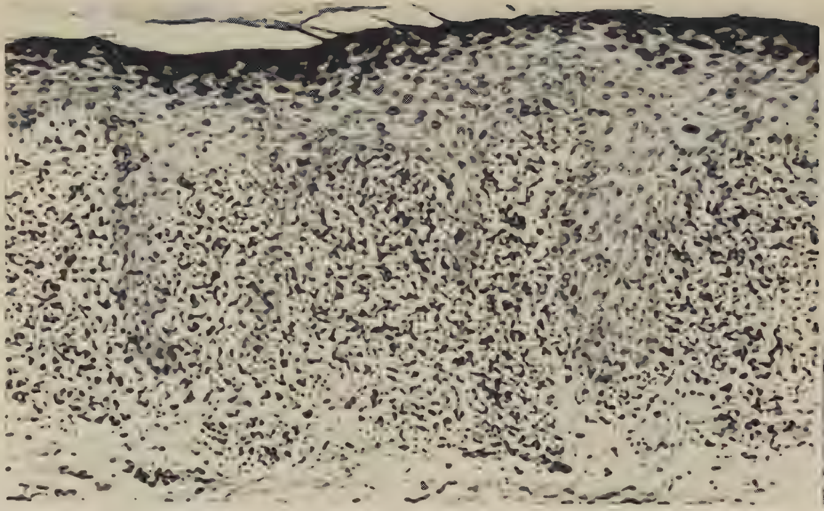
Senile keratosis, on exposed skin surface. Dyskeratotic area (right) and more normal epidermis at left. x48.



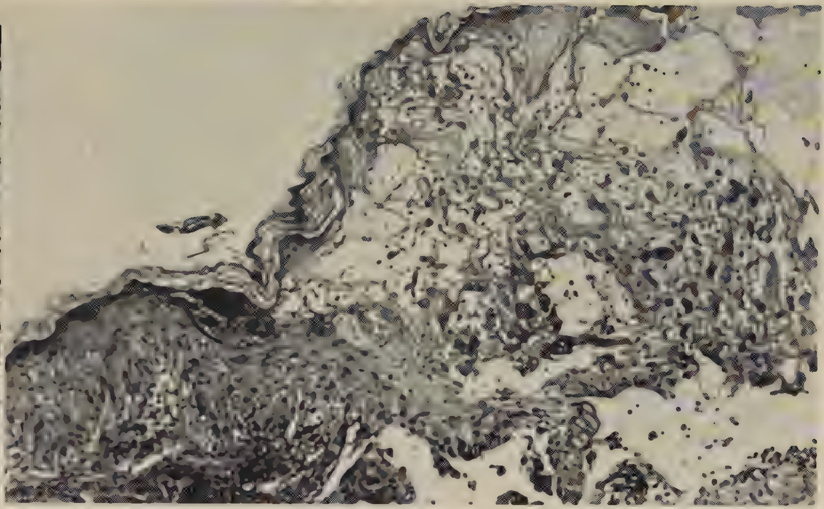
Bowen's disease. Loss of polarity; atypical cells, numerous giant and multinucleated cells. Clear cytoplasmic zone around nucleus may simulate Paget cell. x125.



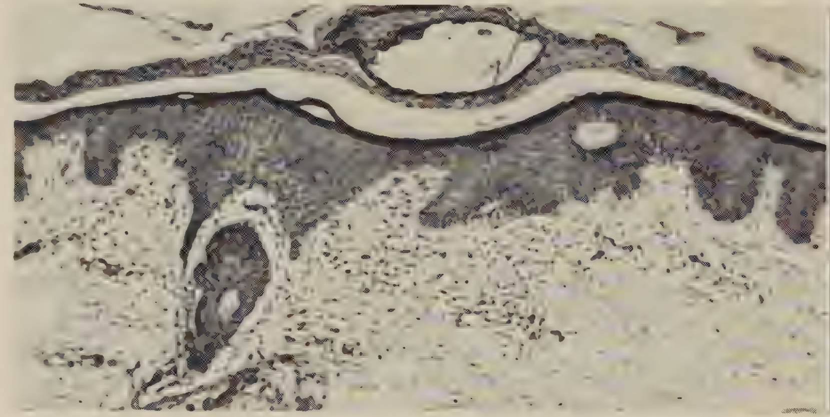
Arsenical keratosis. Histopathologic features are those of other malignant dyskeratoses. Atypical epithelium extends into dermis. x185.



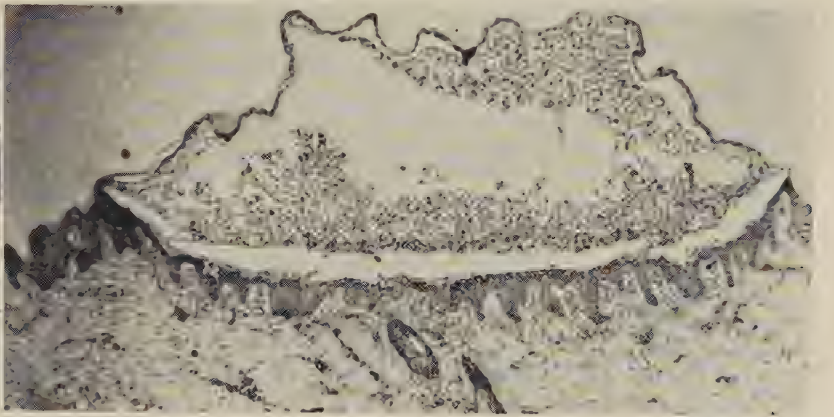
Lichen planus. Hyperkeratosis; no parakeratosis; prominent and thickened granular layer; acanthosis, usually with long pointed rete pegs; liquefaction degeneration of basal layer; dense inflammatory infiltrate intimately associated with basal layer and sharply limited to the upper dermis. x 100. Mucous membrane lesions occur with and without cutaneous involvement. Etiology unknown.



Herpes zoster. Margin of typical vesicle: keratin and granular layers of the epidermis form its roof, papillary layer of the inflamed corium, its floor (lower right). Both "reticular colliquation" and "ballooning degeneration," characteristic of virus vesicles, are well shown. x 75. In healing, new epithelial cells grow into the vesicle from bottom and sides. Scars remain in cases of severe involvement of the superficial corium.

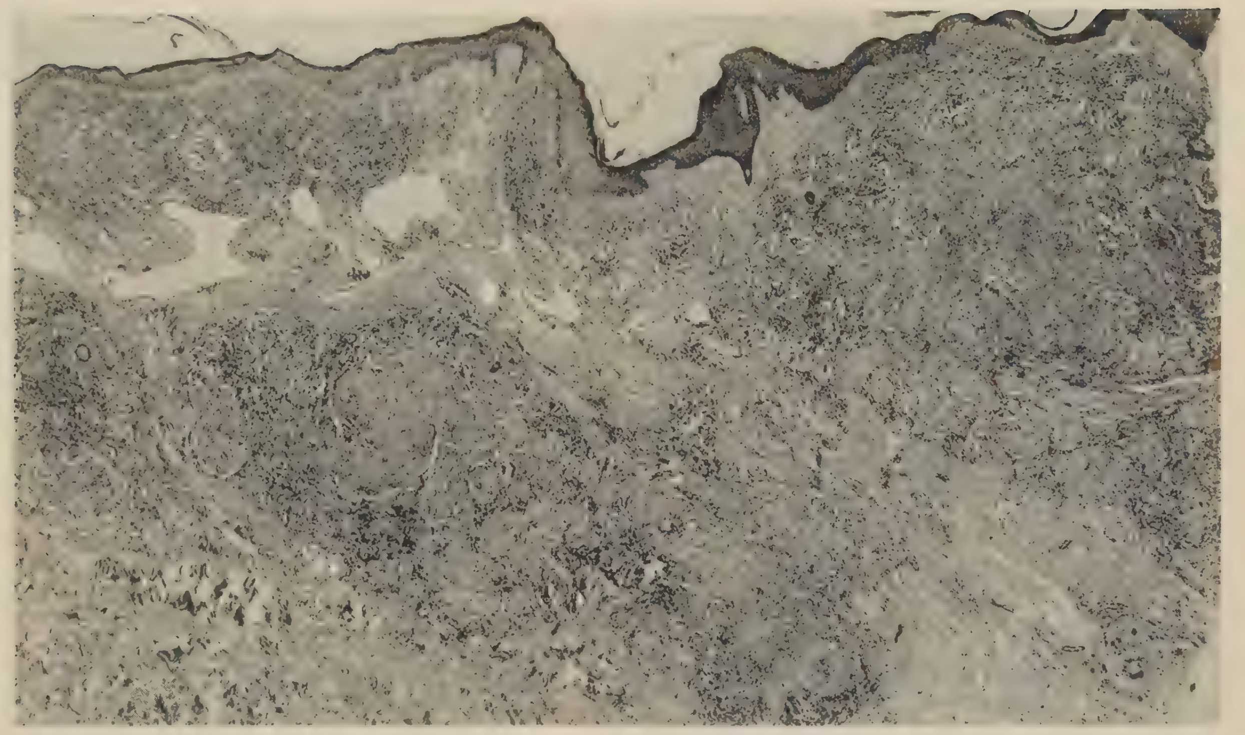


Seborrheic dermatitis. Histologic changes are not specific or diagnostic. Vesicles containing cocci may be found within the stratum corneum in some acute and chronic forms. Parakeratotic scale, slight to moderate acanthosis, dilated vessels, perivascular infiltrate in dermis. Intercellular and intracellular edema are not pronounced in this lesion. Atrophic follicle at left. x 75.

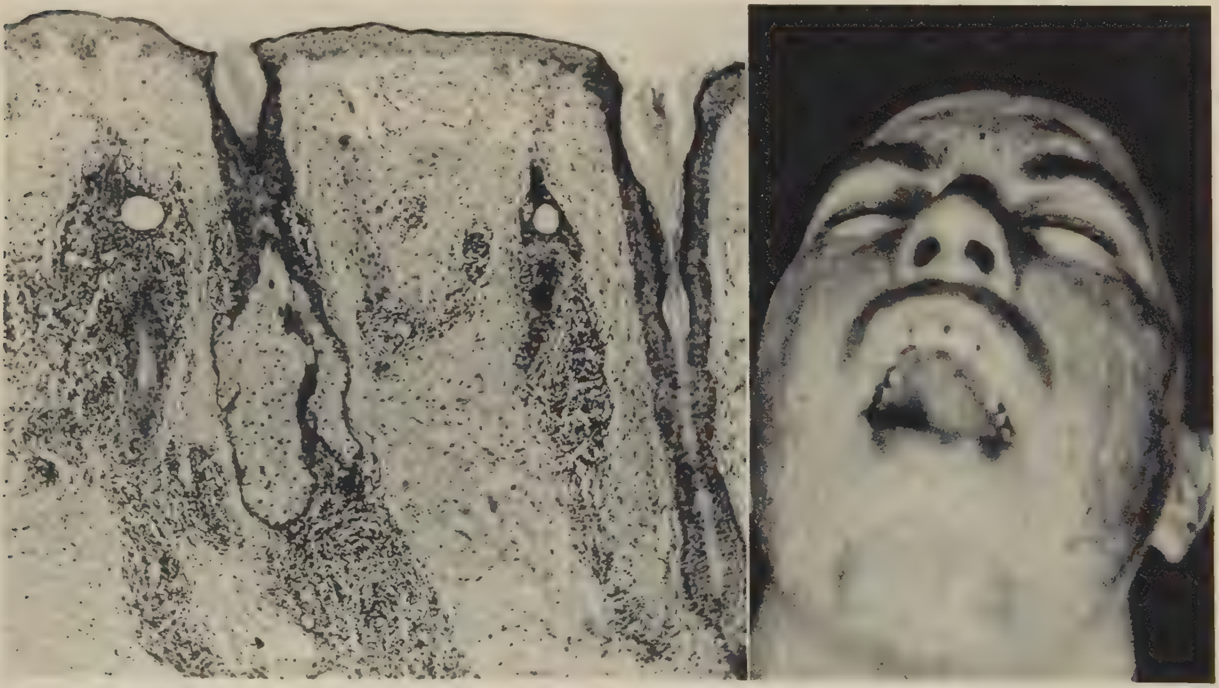


Impetigo contagiosa. Superficial vesicle contains serum, polymorphonuclear leukocytes and cocci. It has formed directly under the keratin layer and the granular layer is its base. Moderate inflammatory cellular infiltrate in underlying epithelium and dermis. x 45.

LUPUS VULGARIS–LUPUS ERYTHEMATOSUS



Lupus vulgaris, most common form of cutaneous tuberculous infection, the course of which is usually slowly progressive. Portions of the epidermis are atrophic; superficial vessels greatly dilated, and the dermis thickened by discrete and diffuse (right) tubercle formation. These are typical, with epithelioid cells, Langhans' giant cells and peripheral zones of lymphocytes. x 25. The skin of the face, particularly about the cheek and nose and the lobule of the ear are favorite sites of attack, and mucous membranes are frequently involved.



Lupus erythematosus. Hyperkeratosis, keratotic plugging of hair follicles and sweat ducts; alternate atrophy and acanthosis of epidermis; dilatation of superficial vessels; edema of the dermis; perivascular mononuclear exudate about skin appendages; and liquefaction degeneration of the basal cell layer. x 55. The disseminated type has involved not only the face, but the oral mucosa. This form occurs predominantly in the female.

CHAPTER 10

TUMORS OF THE SKIN

SEBACEOUS ADENOMAS

Sebaceous adenomas are seldom neoplasms but result from hypertrophy of sebaceous glands already in the part. There are several clinical forms. One of the less common, the Pringle type, occurs as part of a general dystrophy manifested in association with feeblemindedness, tuberous sclerosis, and other evidences of maldevelopment. It is seen in children and young adults as multiple tumors of the face and body, most numerous over the cheeks and nose. They are firm papules, from pinhead to pea-sized, that are usually associated with fine telangiectases. It is possible to have this skin feature without the mental disturbances.

Another uncommon type is a nevoid lesion, either single or multiple, that is not associated with the mental defects, and histologically shows the presence of nevus cells in addition to the sebaceous glands. This is a rare type of nevus.

The commonest form is the SENILE SEBACEOUS ADENOMA. This develops later in life as one of the manifestations of senile change of the skin. It occurs chiefly on the forehead but also on the face. It is a small, flat, firm, yellowish papule, usually without associated inflammatory reaction. Because of the widely dilated follicles it is umbilicated and may be confused clinically with molluscum contagiosum.

Histologically, the lesion consists of hypertrophied sebaceous glands which lie in the superficial part of the dermis, grouped about a greatly dilated follicle that is filled with keratinous and sebaceous debris. The epithelium of the follicle is usually acanthotic and at times shows the malignant type of dyskeratosis seen in leukoplakia, which in rare instances results in squamous cell or basal cell carcinoma. There is usually a mild, restricted, chronic inflammatory reaction around the follicle. If the sebaceous glands rupture with escape of sebum into the tissue, the resulting foreign body granuloma can be mistaken for tuberculosis. Associated collagenous degeneration and elastosis of the dermis always represent additional senile changes.

Rhinophyma is the important sebaceous-gland lesion to the otolaryngologist. It is an extreme example of hypertrophy of sebaceous glands which involves especially the glands of the alae of the nose. The process eventually develops into an enormous, nodular, glossy enlargement of the lower portion of the nose—*pfundnase*. It occurs predominantly in adult males and there is usually a history of longstanding rosacea—"rum blossom," which is essentially a telangiectasia with a varying acneiform component. The developed lesion is not necessarily confined to the nose but may extend to the contiguous tissues of the lips and cheeks. There is no difficulty in the clinical diagnosis of full blown rhinophyma. In addition to the lobulated enlargement of the nose, enormously dilated follicles can be detected.

Microscopically, the dermis is closely packed with hypertrophied sebaceous glands, all well developed and well differentiated. The tremendous enlargement results not only from hypertrophy of the lobules, but also from hyperplasia and actual increase in the number of glands and lobules. Acanthosis and hyperkeratinization in the follicles are prominent features as in the simple senile adenoma. Commonly found in the debris of the follicular contents is the larval mite *Demodex folliculorum,* a harmless saprophytic parasite.

With time, there is an increase in fibrosis of the dermis with some atrophy of both the sebaceous glands and the vascular elements so prominent in the earlier phases. There is a mild chronic inflammatory reaction of plasma cells and lymphocytes. The process is benign and can usually be eradicated by plastic surgery.

BENIGN TUMORS

In addition to the sebaceous adenomas just discussed and to carcinoma, leiomyoma, keloid, and vascular tumors presented in other sections, there are several benign tumors occurring in the skin of the face that should be mentioned.

A great variety of tumors arise in the sweat gland and its anlage. The simplest is the **syringocystadenoma** that consists of a collection of dilated ducts and glands. The embryonal tumors present a varied and complicated histologic series including masses of recognizable gland elements, cysts filled with papillary elements, undifferentiated masses of cells in varying proportions. In spite of the disturbing histologic picture they may present, they are, for general purposes, benign. Occasionally, however, frank adenocarcinoma of sweat-gland origin does occur.

A confusing nomenclature has developed because of the varied histologic picture—syringadenoma, cylindroma, hydradenoma, nevus syringocystadenomatosus papilliferus, and turban tumor, as examples. The last has the added feature of collagenous bundles among the epithelial elements. Its name is derived from its location in the scalp where it may be multiple and cover large areas.

Not infrequently, mucinous and cartilaginous elements in such tumors cause them to resemble the mixed tumor seen in salivary glands. In the Registry are a number of these "mixed tumors" from the lips and skin of the face and neck.

Dermatofibroma lenticulare occasionally develops in the skin of the face. One from the nose is included in the following illustrations.

This is a tumor of fibroblasts, blood vessels, and a varying proportion of lipid-containing histiocytes, occurring most commonly on the legs. It is benign in spite of its irregular cell pattern and histologic invasiveness. It is considered by some to be primarily vascular and as a consequence they refer to it as sclerosing hemangioma. The foamy histiocyte is the prominent feature in some of these lesions and the term histiocytoma has been introduced to describe them. Others regard it not as a tumor but an inflammatory reaction and they have suggested the term nodular subepidermal fibromatosis to avoid the implication that the process is neoplastic.

BASAL CELL CARCINOMA

This tumor, in which the cells generally retain the basal character, occasionally arises from the squamous epithelium of the mucosa, but usually from that of the skin. It is the commonest malignant tumor of the face, but it rarely occurs below the line of the mouth. It is seen about the eyes, root of the nose, on the forehead, temple, malar eminences, and ear. It is the common malignant tumor of the upper lip where squamous cell carcinoma is rare.

It was formerly the custom to divide the basal cell tumors into two groups — the relatively benign Brooke type, or congenital epithelioma adenoides cysticum, and the more aggressively invasive and destructive rodent ulcer, or Krompecher type. The former was assumed to have arisen from a skin appendage, the latter from the basal layer of the surface epithelium. The modern tendency is to drop these eponyms, to recognize as a separate entity the congenital, usually multiple and benign tumor, epithelioma adenoides cysticum, and to consider the malignant tumor as it develops in later life to arise from the special basal cells of the surface epithelium that are potentially skin-appendage cells. This would account for the scarcity of the basal cell tumor in mucosae. The tumor originally described by Brooke was a dysontogenic lesion that included several embryonic skin appendages and did not show the epithelial proliferation of the usual basal cell tumor. The cystic and adenoid features are common in the aggressive adult carcinoma, and there are few of the tumors that do not include foci of differentiation to hair keratin. This indicates that their origin, when not actually from a hair follicle, is from basal epithelium with the potentiality for forming such structures. When the hair differentiation is a prominent histologic feature, the tumor is termed "trichoepithelioma." This carries the connotation of a lower grade of malignancy than the unmodified term "basal cell carcinoma."

There are all gradations of architecture, amount of differentiation, extent of the adenoid and cystic features, and of circumscription. A strictly practical classification, therefore, is not possible. Broadly speaking, the benign congenital lesion is well circumscribed with no invading off-shoots; there is no evidence of active cell proliferation, and the pseudoglandular and cystic features are prominent. The malignant tumor, on the other hand, is made up of irregular masses of basal-type cells that are usually outlined by palisaded, more uniform and taller cells, with isolated strands of undifferentiated cells infiltrating the contiguous tissues. Mitoses are more numerous, differentiation to hair keratin not so prominent. The larger masses of cells may show a lacy pattern instead of the more cystic architecture.

The cystic adenoid feature of the basal cell tumor is seen also in some carcinomas of respiratory epithelium, in bronchial adenomas, and in mixed tumors of the salivary-gland type. The terms "cylindroma" and "basaloma" have been applied to such tumors.

Basosquamous cell carcinoma.—In basal cell tumors it is not uncommon to see groups of cells that have differentiated to the squamous type. This has already been mentioned in connection with the tendency to differentiate further to hair-shaft keratin. The presence of such well differentiated squamous cells does not, however, make the tumor a basosquamous carcinoma, because the only malignant element is the basal cell. Occasionally, however, the squamous-epithelial component does show the malignant characteristics of pleomorphism, atypical mitotic figures, and invasion of the stroma. Such a tumor can then correctly be termed basosquamous carcinoma. This is of more than academic importance, for the malignant squamous cell element in this tumor may metastasize, something that the pure basal cell tumor does not do. This tumor most frequently develops about the eyes and the root of the nose.

NEVUS

The term **nevus** may be applied generically to any congenital defect in the skin, but it is more often used in a restricted sense to designate those dermal lesions that are made up of the melanin-forming cells, the melanoblasts. Such tumors are the pigmented nevi and they occur in a variety of clinical and pathologic forms. They are usually multiple and may occur as flat areas with varying degrees of pigmentation, singly, or in rows apparently following the course of a nerve. Nevi may cover large areas of the body including the face, but the more verrucous type is less apt to be extensive. The verrucous forms are usually more heavily pigmented than the flat moles and they may be associated with other developmental defects in the skin, including hypertrophied hair follicles or those of the lanugo type, embryonal sweat glands or, more rarely, sebaceous glands.

The origin of the nevus cell is still a matter of dispute, but it is convenient to assume that it comes from the neural ectoderm of the primary neural crest and that it reaches the periphery in the nerve sheaths along with the Schwann or neurilemma cells.

Histologically, there are four chief types of nevi that concern us:

1. The common INTRADERMAL NEVUS in which the nevus cells are arranged in groups and cords and are confined to the true skin. For practical purposes this form of nevus is always benign.

2. The more deeply lying tumor which includes stellate and multinucleated cells. These cells frequently show a disconcerting pleomorphism and usually contain considerable melanin. Some of the cells may be arranged in groups that suggest the attempt to form Meissner's corpuscles, a distinct evidence of neural origin. Because these cells are deep in the dermis, these nevi appear clinically as blue spots and are called BLUE NEVI. These, also, are generally benign, but occasionally a malignant type has been reported.

3. The third form is usually still deeper in the dermis. The nevus cells are closely associated with nerve fibers and at times with even more highly organized neural elements than those seen in the blue nevus. This type is called NEURONEVUS and is a perfectly benign tumor.

4. The fourth form, the INTRAEPIDERMAL, DERMOEPIDERMAL, or JUNCTIONAL NEVUS, is characterized by the presence of nevus cells in the basal layer of the epidermis, either singly or in small groups. The cells are round with centrally placed, dark nuclei and the cytoplasm is characteristically clear, in fact, they were specifically termed clear cells by Masson. Groups of similar cells are usually present in the underlying dermis associated with spindle cells that are usually more heavily pigmented. This is the potentially malignant nevus from which the malignant melanoma develops. This tumor assumes a variety of cell patterns. Some retain the mixture of spindle and epithelial cells and varying amounts of pigment; others consist only of the epithelioid type of cell and contain no pigment. This unpigmented tumor is sometimes spoken of as amelanotic melanoma or melanocarcinoma. We prefer the term malignant melanoma for all tumors that develop from the nevus cell.

A special note about nevi in children is necessary. These frequently are of the intraepidermal or potentially malignant type, but it is very rarely, even with this histologic character, that they behave as clinically malignant tumors before puberty. With the onset of puberty, however, the situation rapidly reverses and it is not uncommon for such a tumor to produce widespread metastasis in patients below twenty.

Nevi of any type may come to the attention of the otolaryngologist because they are present on the face, ears and neck, and he should have at least this working knowledege of their pathology and potentialities. Nevi do occur in the mucosae, but they are rare. One removed from the base of the right anterior faucial pillar is included among the following illustrations. Several instances of malignant melanoma primarily in the upper respiratory mucosa are included in the section on malignant tumors of the upper respiratory tract.

Other dermatoses are discussed in the sections on the external ear, on the fungus diseases and on the tropical diseases.

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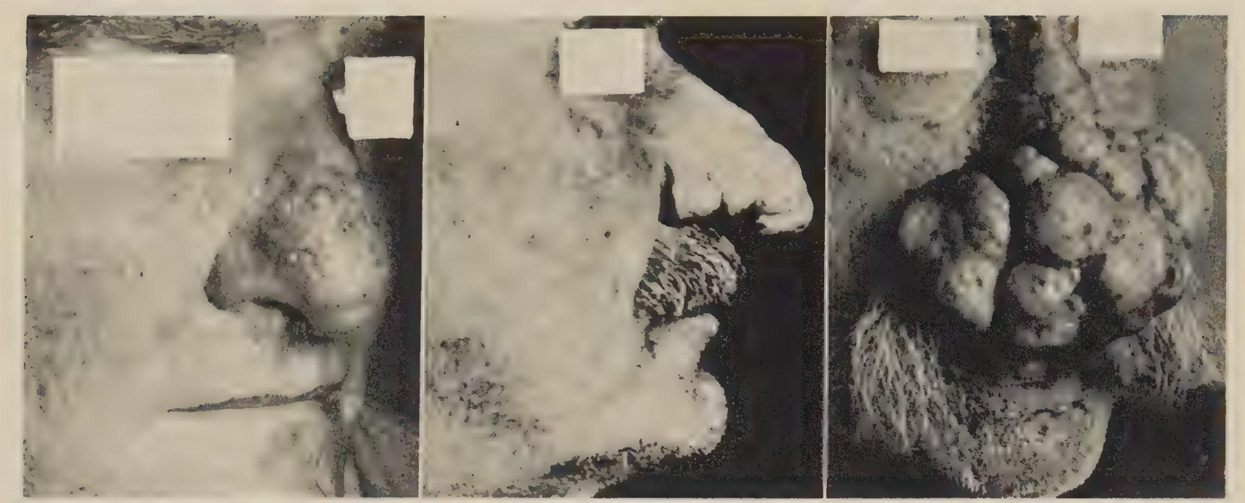
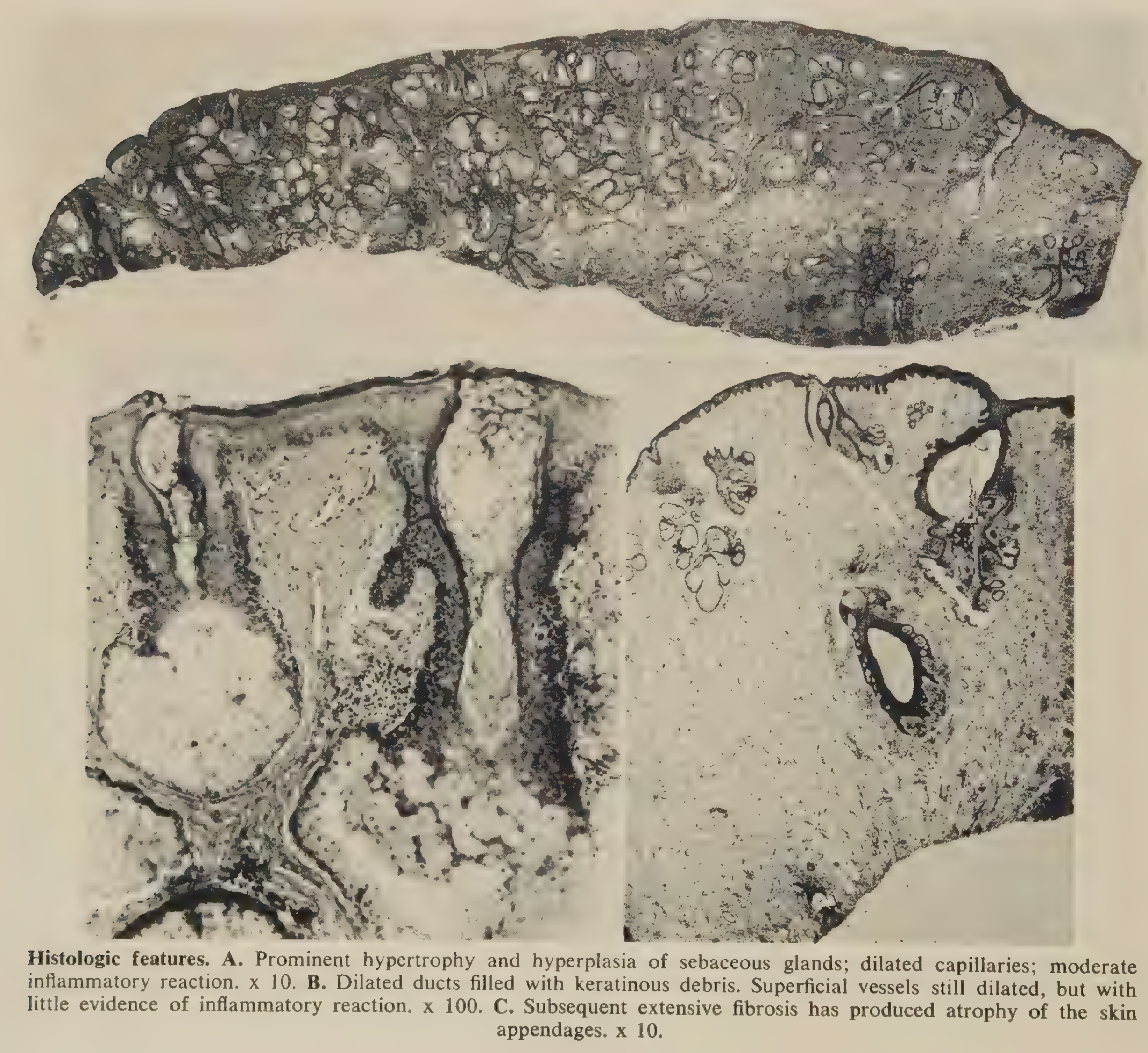
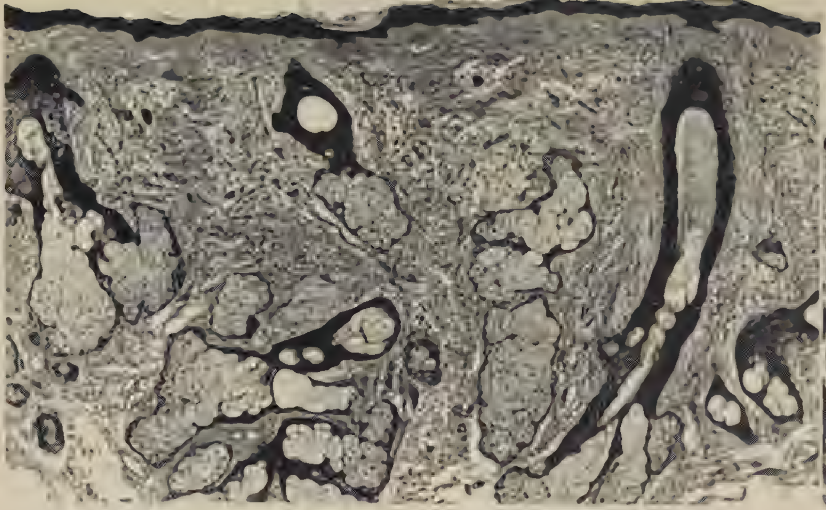


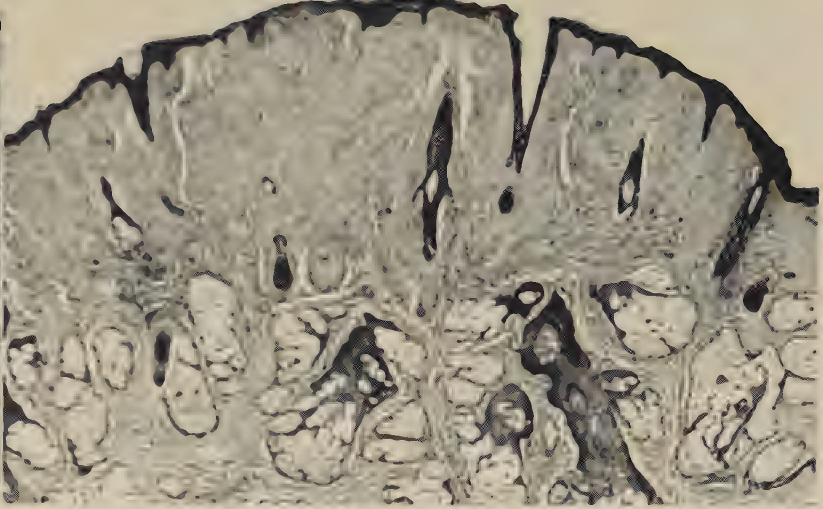
Rhinophyma. Three clinical phases are illustrated. **1.** Rosacea, with telangiectasia, papular acneform lesions; red, shiny, thickened skin. **2.** Striking hypertrophy of nasal tissues. **3.** Lobulated pendulous masses–pfundnase.



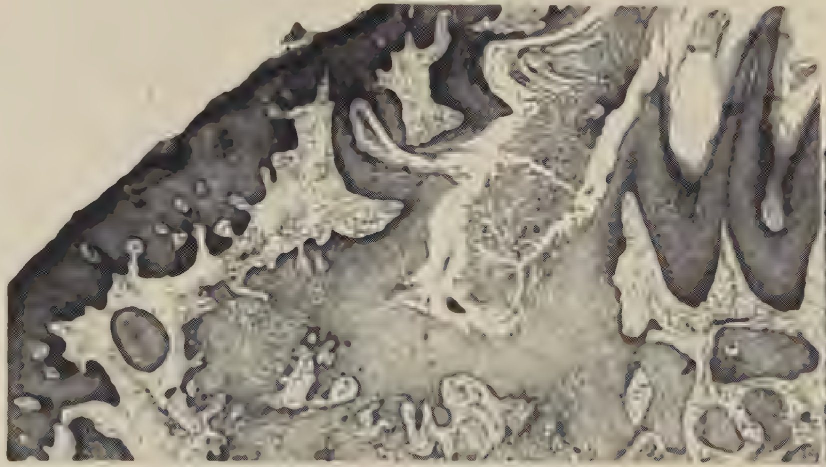
Histologic features. A. Prominent hypertrophy and hyperplasia of sebaceous glands; dilated capillaries; moderate inflammatory reaction. x 10. **B.** Dilated ducts filled with keratinous debris. Superficial vessels still dilated, but with little evidence of inflammatory reaction. x 100. **C.** Subsequent extensive fibrosis has produced atrophy of the skin appendages. x 10.



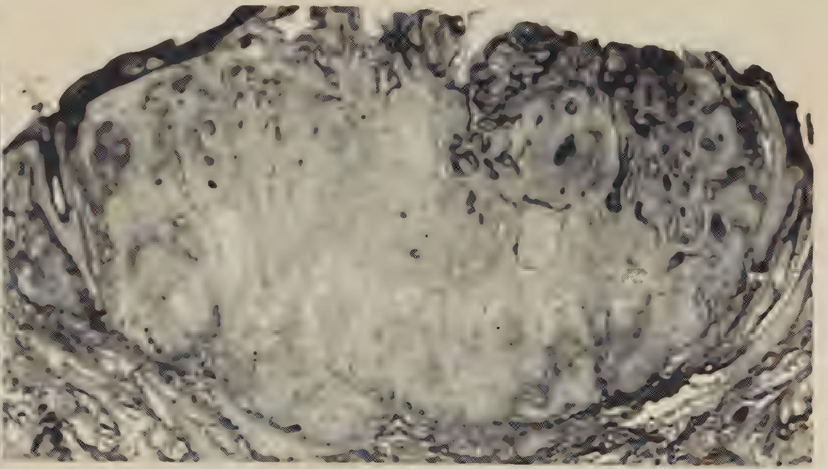
Senile sebaceous "adenoma." Hypertrophy of sebaceous glands, but no increase in number; not a neoplasm. Other senescent changes in skin are evident: atrophy and more frequently acanthosis of epidermis; degeneration of collagen and elastic tissue of dermis. Usually some inflammatory reaction. x 48.



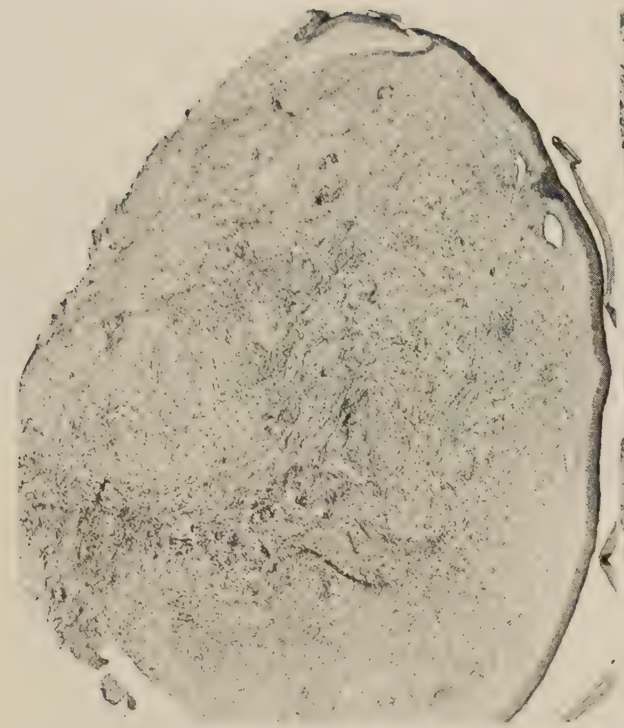
Juvenile or nevoid sebaceous "adenoma." Actual increase in number of sebaceous glands and of fibrous tissue, occurring at an early age. Often reported in mentally deficient patients, and with other skin defects such as warts, nevi, pigmented spots. x 34. (Both from W. Dolan, Arlington, Va.)



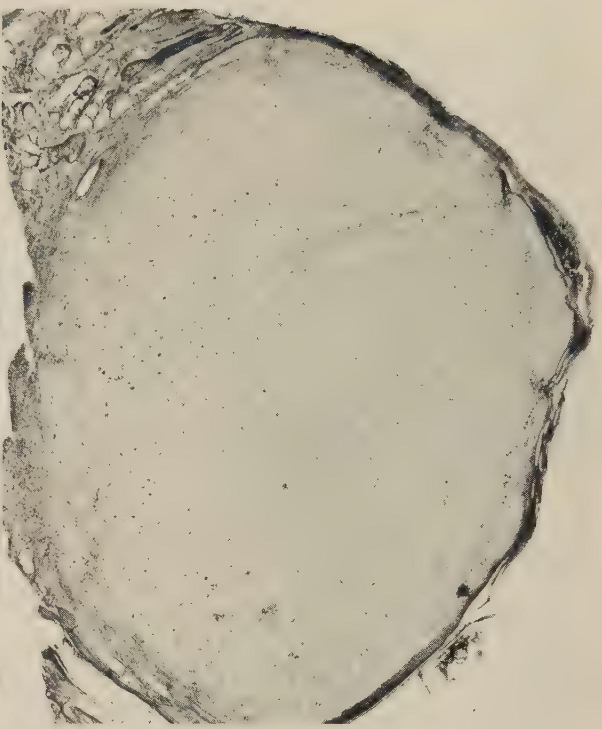
Non-specific keratosis of follicular structure. Frequently noted in senile skin, especially of face. Hyperkeratosis and marked pseudoepitheliomatous hyperplasia of epithelium of hair follicle. x 50. The term "follicular keratosis" is accepted as a synonym for Darier's disease and should therefore *not* be applied to this lesion.



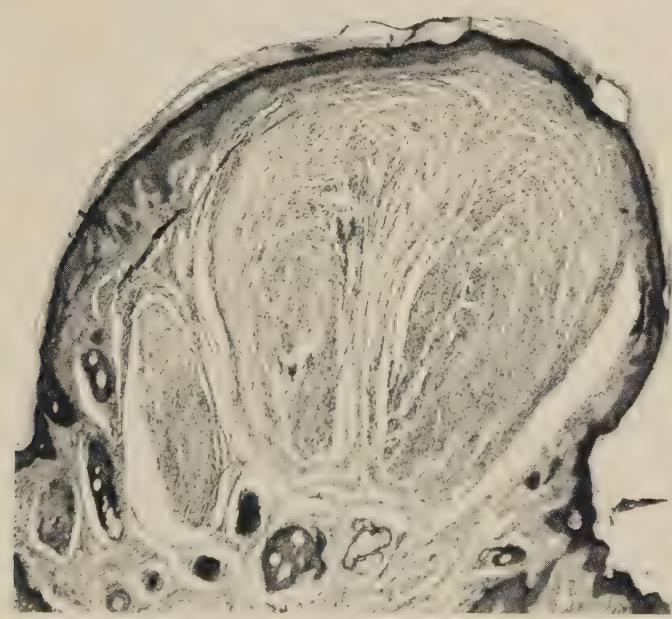
Inverted follicular keratosis (inverted papilloma), most common on nose. A circumscribed mass with well-defined base. Composed of winding, occasionally whorled strands of acanthotic epithelium of obvious hair follicle origin, the cells of which show orderly maturation from basal to squamous type. Benign. x 200.



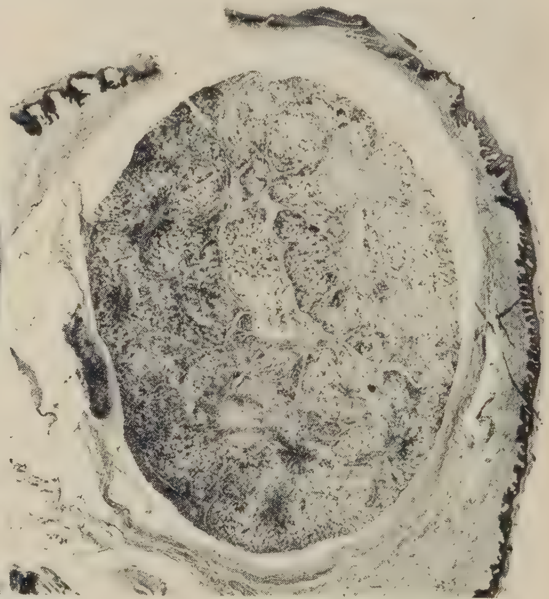
Dermatofibroma lenticulare (sclerosing hemangioma; subepidermal nodular fibrosis). Poorly defined mass of fusiform cells and whorled collagen bundles. May contain hemosiderin, masses of foamy histiocytes and few or numerous thick-walled blood vessels. Thin subepidermal clear zone between lesion and atrophic epidermis. x 30.



Nevoxanthoendothelioma. Subepidermal elevated circumscribed nodule extending to mid-corium, made up predominantly of large cells with foamy cytoplasm and fibrovascular tissue. The very numerous giant cells, most of the characteristic Touton type, appear as small dark spots. x 16.

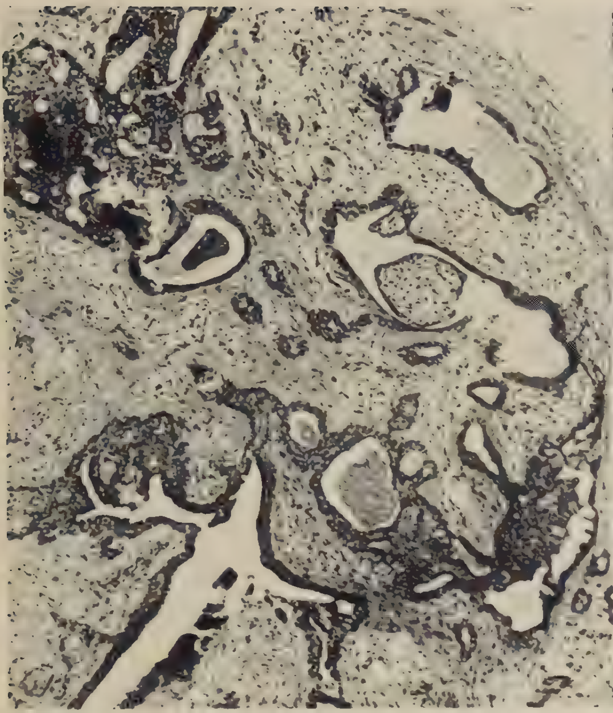


Neurofibroma. Elevated nodule containing unencapsulated mass composed of irregularly arranged bundles of fibers. Special stains usually demonstrate the presence of nerve fibers as an integral part of this tumor. x 34.

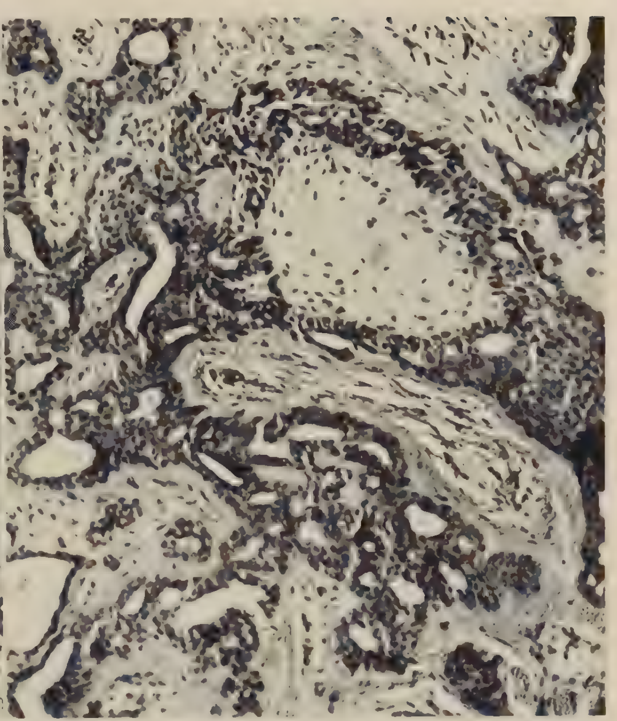


Neurilemoma. Well encapsulated mass composed of interlacing bundles of fibers in which alternating rows of parallel cells and anuclear parallel fibers produce characteristic "palisaded" pattern, evident even at this very low magnification. x 11.

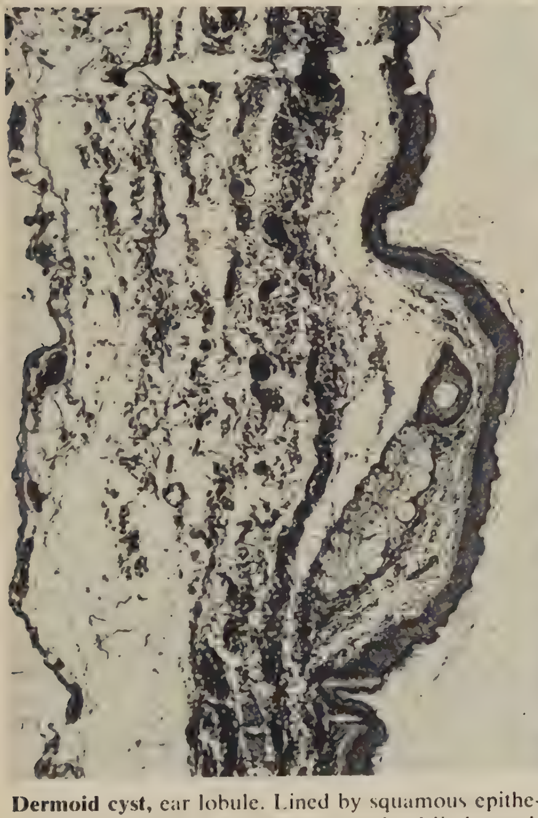
BENIGN TUMORS–METASTATIC TUMOR



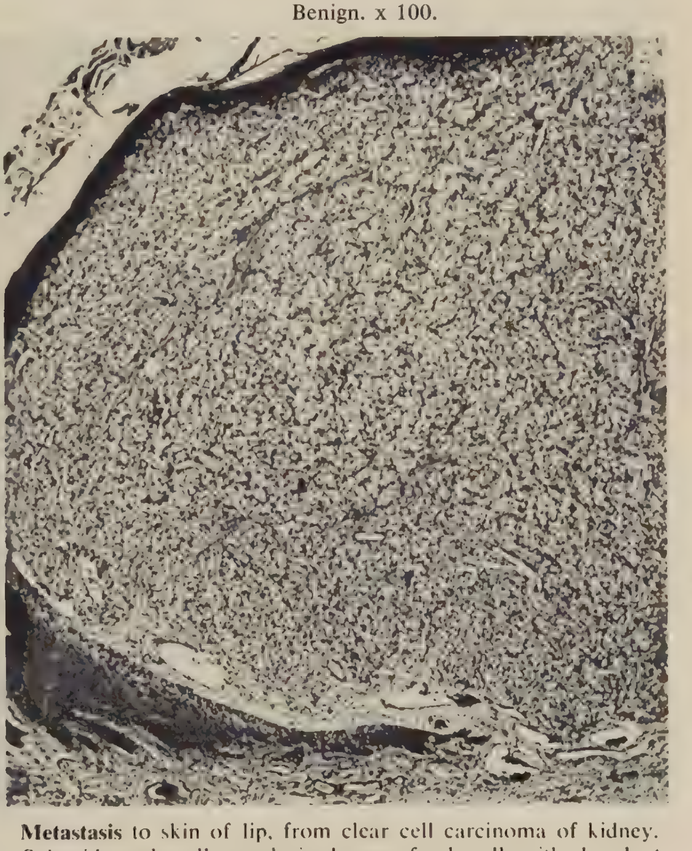
Syringadenoma, nose, developing from sweat gland. Assumes a wide variety of forms. Benign. x 62.



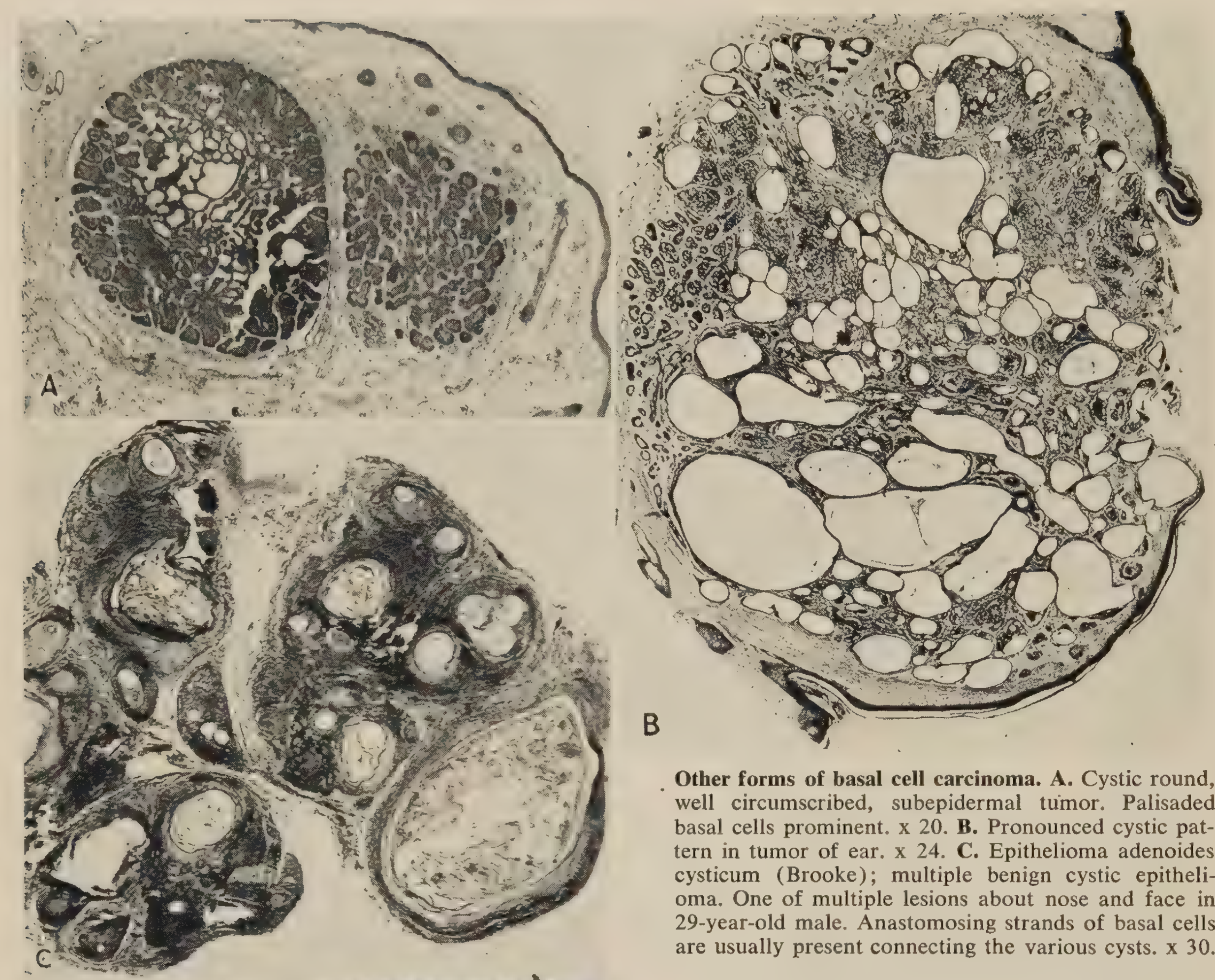
Mixed tumor (adenoma) of sweat-gland origin, skin of nose. Adenomatous elements and an island of chondroid tissue. Benign. x 100.



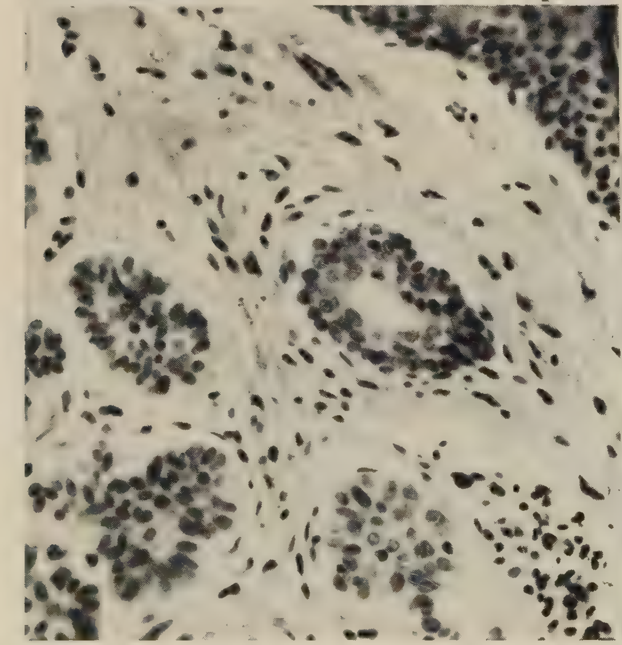
Dermoid cyst, ear lobule. Lined by squamous epithelium. A hair follicle and sebaceous gland lie beneath the epithelium. Benign. x 62.



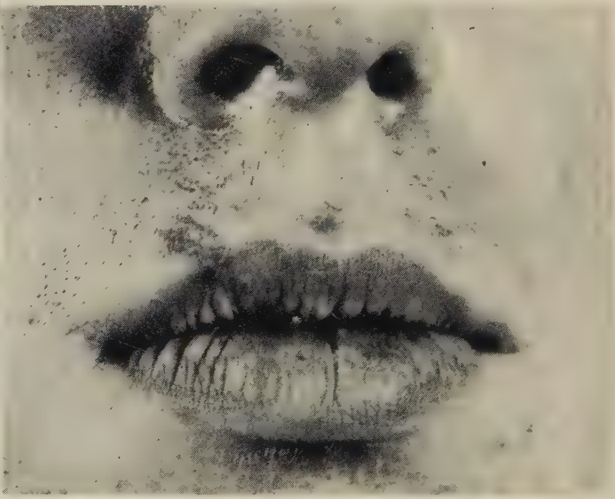
Metastasis to skin of lip, from clear cell carcinoma of kidney. Subepidermal, well vascularized mass of pale cells with abundant clear cytoplasm. x 40.



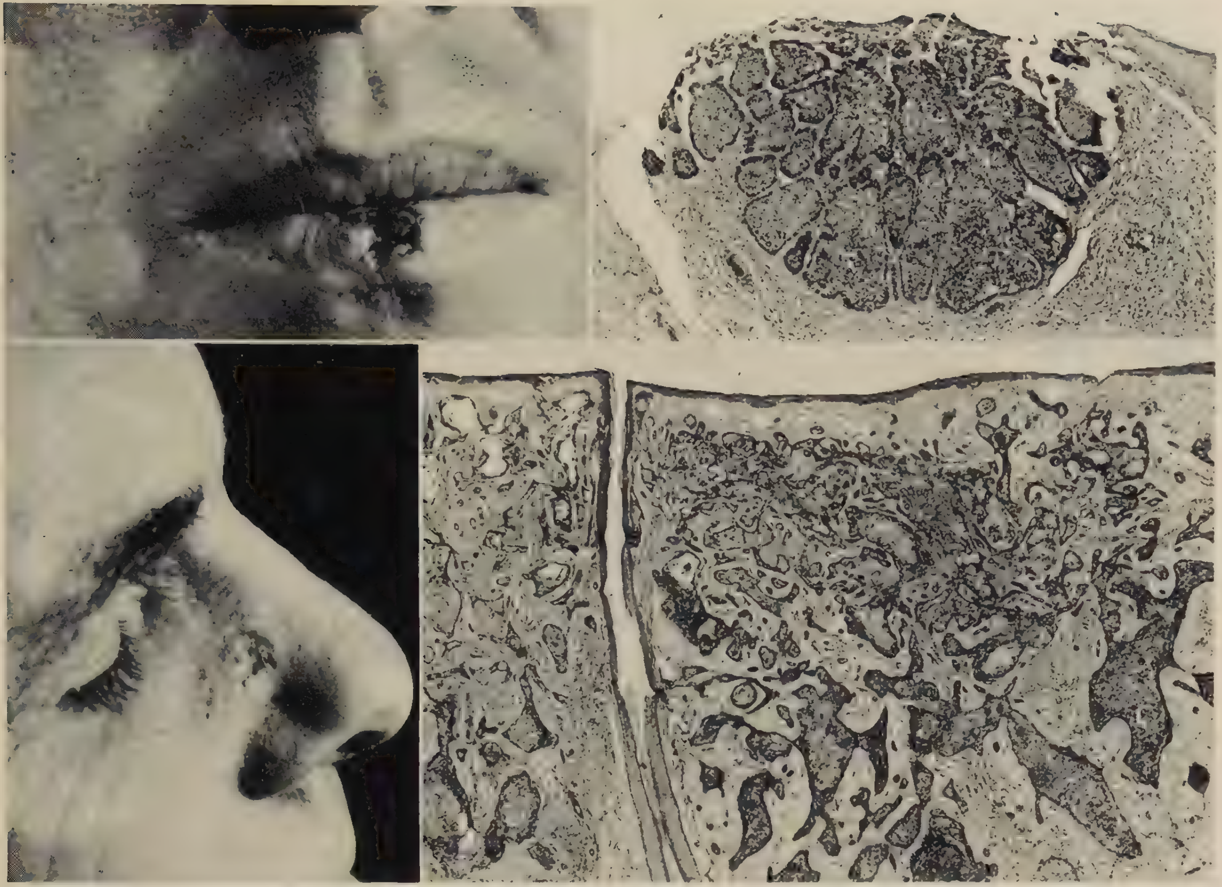
Other forms of basal cell carcinoma. A. Cystic round, well circumscribed, subepidermal tumor. Palisaded basal cells prominent. x 20. **B.** Pronounced cystic pattern in tumor of ear. x 24. **C.** Epithelioma adenoides cysticum (Brooke); multiple benign cystic epithelioma. One of multiple lesions about nose and face in 29-year-old male. Anastomosing strands of basal cells are usually present connecting the various cysts. x 30.



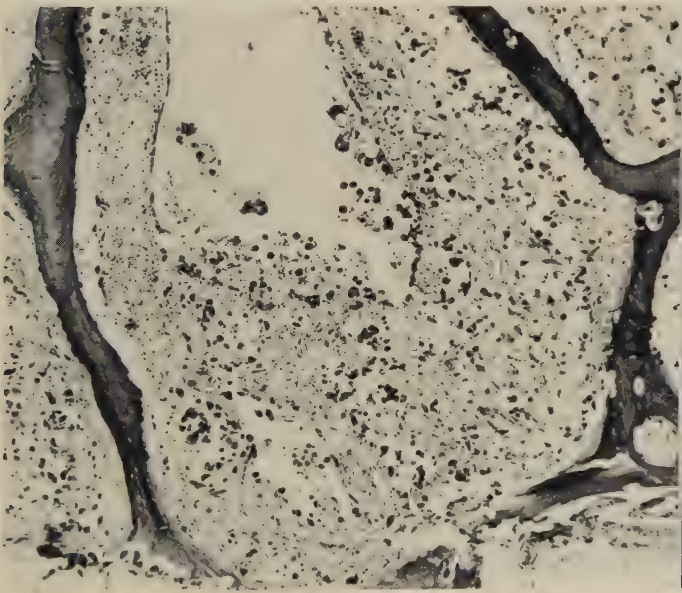
Basal cell carcinoma. Small groups of cells simulating adnexal structures. x 300.



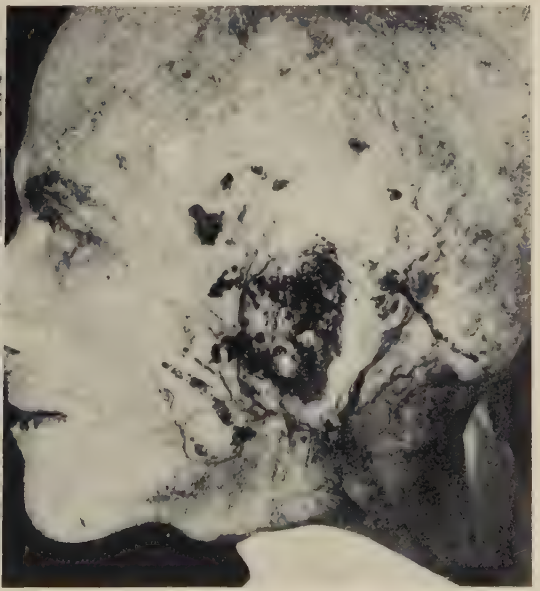
Basal cell carcinoma, upper lip of a 20-year-old male. This tumor practically never occurs on lower lip.



A. **Tuberculosis,** lower lip, readily mistaken for carcinoma or chancre. B. **Basal cell carcinoma,** nose, a common site. A crater with elevated skin margin. C and D. Examples of invasive types of basal cell carcinoma. C, from ear, although ulcerated, is very slowly growing. x 48. D, as yet, not ulcerated, from cheek, has widely infiltrated dermis. x 27.

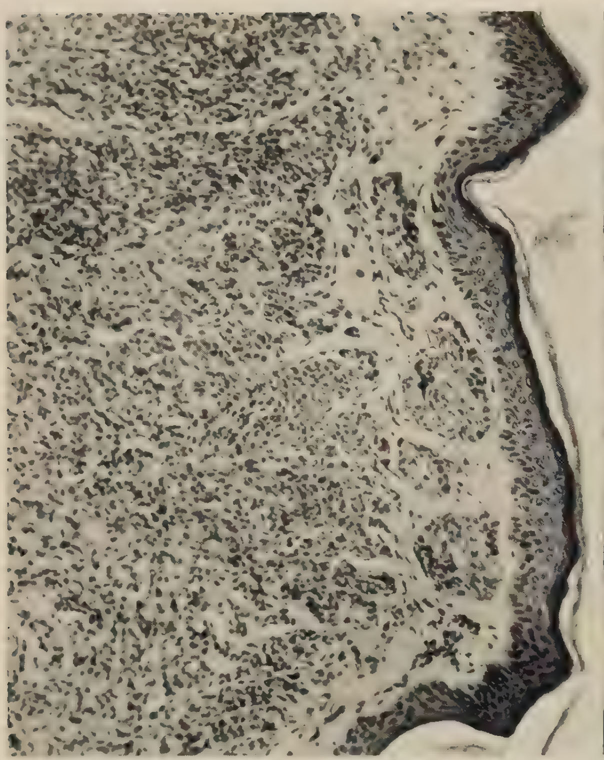


Squamous cell carcinoma of auricle has invaded petrous bone. Pneumatic cell occupied by dissociated pleomorphic neoplastic cells and purulent exudate. x 48.

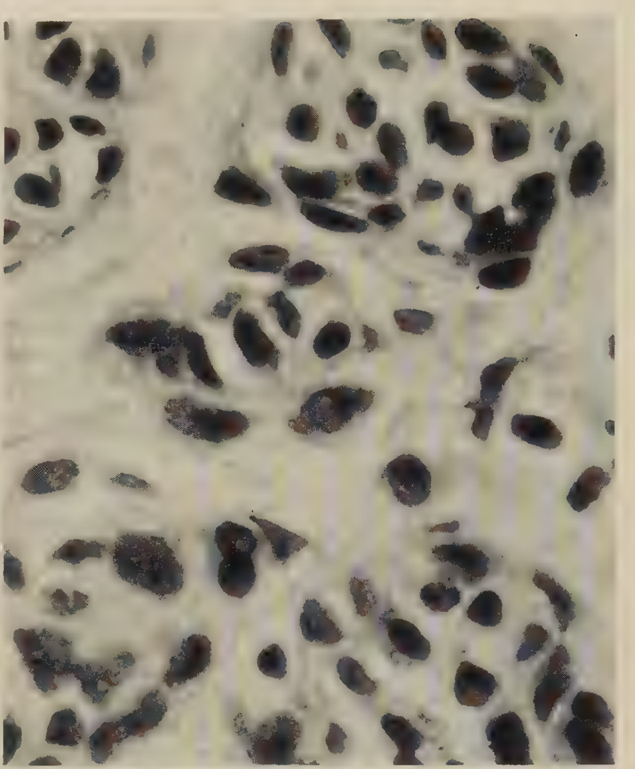


Basal cell carcinoma of ear after years of surgical treatment and irradiation. Skin is atrophic, and nodules of tumor still present.

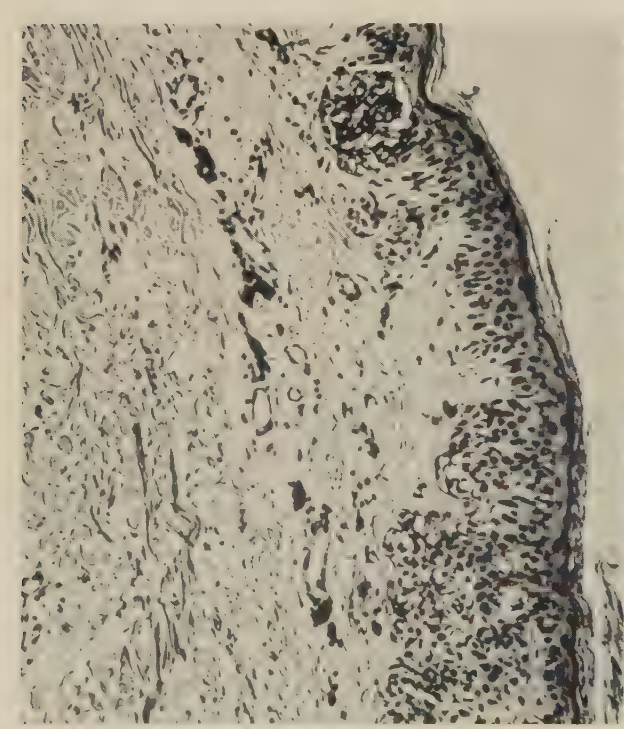
PIGMENTED NEVI–BLUE NEVUS



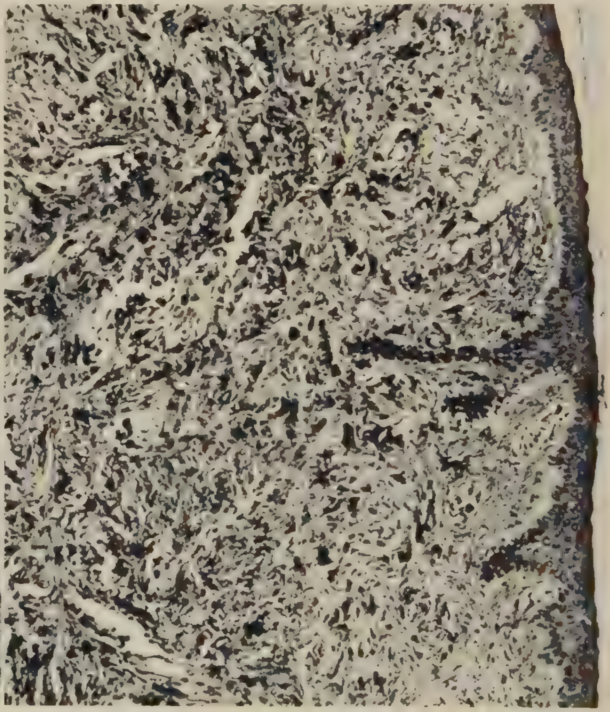
Intradermal nevus. Epidermis is free of nevus cells. Clear zone between nevus and epidermis. Benign. x 75.



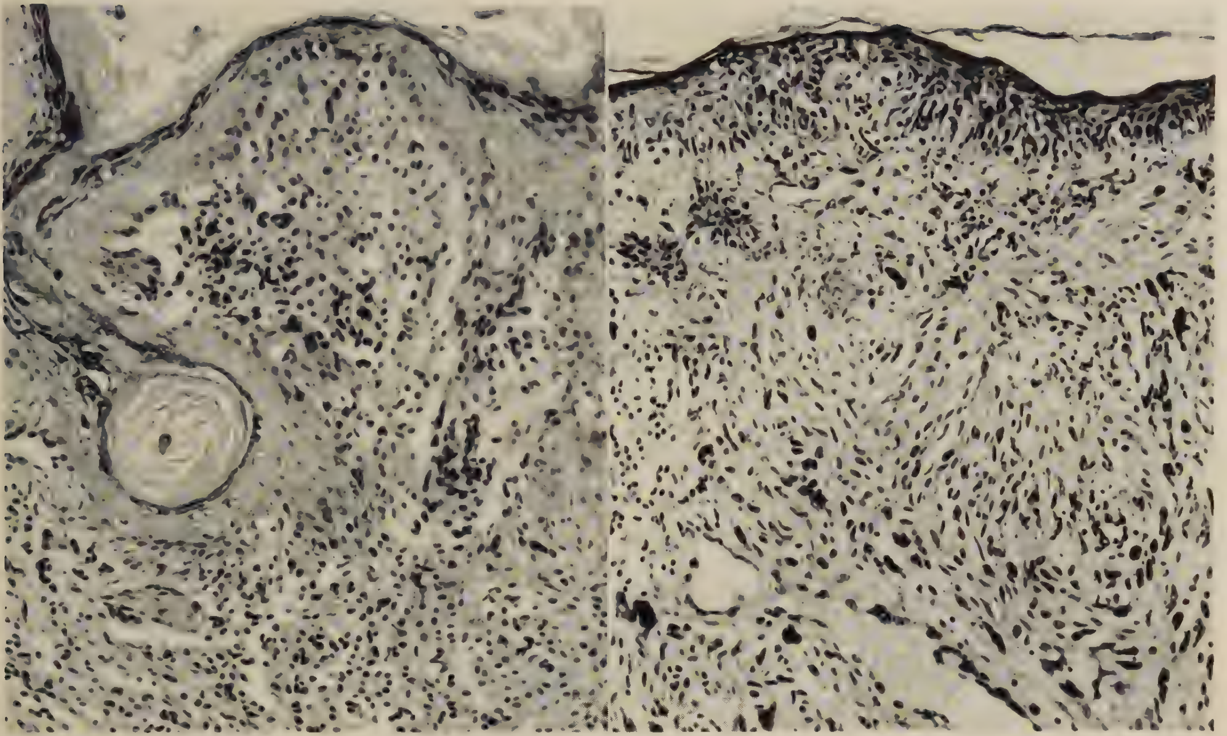
Typical nests of epithelioid, non-pigmented cells. Fairly uniform round and oval nuclei surrounded by pale or clear cytoplasm.



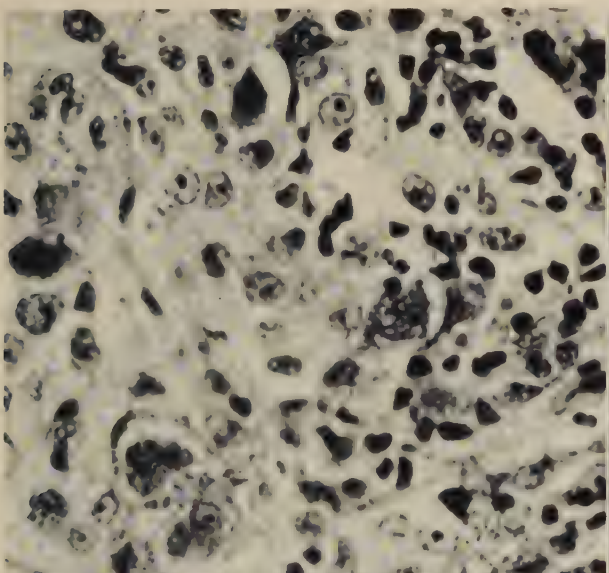
Junctional (dermo-epidermal; marginal) nevus. Clear cells, singly and in clusters, in basal and lower prickle-cell layers of epidermis. A few spindle, pigmented cells in upper dermis. Potentially dangerous. x 100.



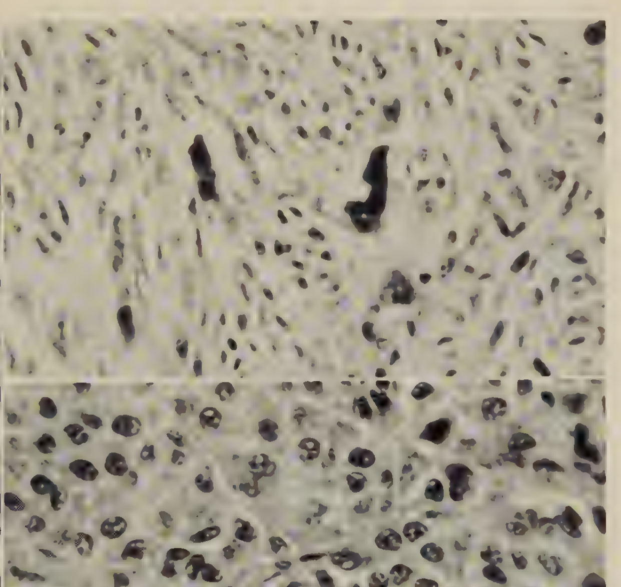
Blue nevus. Clinically, a circumscribed round or oval papule, usually found deeper in dermis than here. Spindle and stellate cells with long processes contain melanin pigment. Very rarely malignant. x 130.



Origin from junctional nevi. A, has undergone malignant change to the epithelial, amelanotic type of melanoma. (x 125); **B,** to the more spindle-cell type with pigmented cells included (x 145). There are nevus cells in the epidermis of both lesions; at right, isolated cells in all layers to the stratum corneum.



Metastasis of a melanoma to the palate. Epithelioid-cell type with bizarre cells of all sizes. x 600.



Metastases from the tumors **A** (at bottom) and **B** (at top). Each has retained essentially the cell type of its parent lesion. x 315.

CHAPTER 11

FUNGUS DISEASES

Fungus infections may be divided into two groups according to their clinical manifestations—the superficial and the deep. No hard and fast line can be drawn between the two, for some fungi usually considered saprophytic or superficial may produce deep focal lesions or become disseminated.

As a rule the superficial fungi are present in mycelial form in the skin and its appendages and the mucous membranes. The mycelia, however, can be only tentatively identified and species determination must be made on the basis of culture. The presence of spores and mycelia can be demonstrated in sodium or potassium hydroxide mounts of skin scrapings. Recently it has been found that the periodic acid-Schiff reaction brings out the morphologic details of the fungi in smears and tissue sections.

Discussion here will be limited to fungus diseases encountered in the field of otolaryngology.

SUPERFICIAL INFECTIONS

Fungi of the dermatophyte group invade only the superficial skin and its appendages. According to Emmons the three genera to be considered in this category are *Microsporum, Trichophyton* and *Epidermophyton*. Because the same organism may be the cause of a variety of clinical manifestations and many dermatophytes of different species and genera can produce the same clinical entity, the infections are designated by the part of the body affected. Tinea pedis and tinea ungium, the commonest of these, are not pertinent to our field.

Tinea capitis (ring worm of the scalp). This condition occurs chiefly in children and is characterized by patchy alopecia, fragmentation of infected hairs, and a fine scaliness of the skin. As is the case in all of the superficial fungus diseases, secondary infection is a common complication, and may result in a severe pyoderma or cellulitis, especially in infections of the hairy skin. The clinical term KERION is applied to the pyoderma which results from fungus infection. The fungi usually identified in this form, which so frequently occurs among school children, are *Microsporum Audouini* and *Trichophyton tonsurans*.

Histologically, the organisms are seen to invade the stratum corneum of the skin and the hair follicles with subsequent involvement of the hair shafts. The accompanying reaction may be very slight, with only the formation of superficial scales between which mycelial threads and spores can be identified. More severe reactions lead to the formation of abscesses in the tissues surrounding the hair follicles.

Tinea favosa (favus), the most serious of the hair infections, is caused by *Trychophyton Schoenleini, T. violoceum* or *Microsporum gypseum*. Uncommon in the United States, it is characterized clinically by the development of sulfur-colored crusts (scutula), which generally occur over the scalp with considerable matting of the hair shafts, and result in alopecia. These scabs are adherent, hemorrhagic and pustular. Tissue destruction may be sufficiently deep to result in scarring.

Histologically, the scutulum is composed of layers of keratin, mycelia and spores. The hair shafts are invaded also and appear as flaky structures. There is usually a severe, although superficial inflammatory reaction in the dermis, but in the uncomplicated cases the reaction in the dermis is relatively slight in view of the severe clinical manifestations.

Favus is very refractory to treatment and will recur even after epilating doses of irradiation.

Tinea barbae is the term applied to fungus infections on the bearded areas of the face. The same organisms are involved as in tinea capitis and tinea circinata. It may result clinically in either a localized lesion or a diffuse infection accompanied by pyoderma. Clinically, the diffuse form closely resembles the purely pyogenic sycosis barbae.

Tinea glabrosa, or ring worm of the glabrous or smooth skin, is usually less severe because secondary bacterial infections are less likely. The infection usually manifests itself clinically as a scaly, circinate patch which spreads peripherally, leaving a clean center. It is from this pattern that the group has attained its name, ring worm. The causative species are the same as those of tinea capitis.

Tinea versicolor is a refractory skin infection caused by *Malassezia furfur*. It involves the covered portions of the body, especially the neck, upper trunk and flexor surfaces of the arms. The legs are rarely involved. The lesions are macules of varying sizes up to that of a quarter, fairly well circumscribed, with a finely furfuraceous surface. It gets its name from the shades of color in the different patches. Usually of faint buff color, they are also red and dark brown. There is little accompanying discomfort, but the infection is refractory to treatment, and relapses are common after it has been apparently cured.

The diagnosis is readily established by the identification of clusters of thick-walled, round and budding forms surrounded by short fragments of mycelium in scrapings from lesions in potassium hydroxide solution or in stained sections of skin.

A number of fungi are capable of reacting on the human or animal body in several different ways. Often behaving as harmless saprophytes, they may produce superficial lesions or occasionally disseminate with fatal effect. Among these are *Candida, Aspergillus, Geotrichum* and *Mucor*. All of them produce lesions in the mucous membranes and thus are of particular interest to the otolaryngologist.

Thrush is the superficial infection of the buccal mucosa caused predominantly by *Candida (Monilia) albicans*. It is most common in infants and children. The lesions are superficial, white, curdled milk-like patches which can be readily removed to reveal a hyperemic, petechial mucosal surface. The infection may extend into the pharynx and down the esophagus and gastrointestinal tract and ultimately prove fatal.

Histologically, the surface epithelium is scaly and its most superficial layers are invaded by the fungus. The reaction in the subepithelial mucosa is more intense than that usually seen in superficial infections of the skin. The fungus *C. albicans* can be seen as a small, oval, thin-walled, budding, yeastlike cell, with or without mycelia, in potassium hydroxide preparations and in periodic acid-Schiff or gram-stained smears of material from the lesions. In tissue sections treated by the periodic acid-Schiff method the fungus elements are prominent.

Candida may be a secondary invader in other mouth conditions such as sores produced by dentures and perléche, a clinical syndrome involving the lips. Saprophytes as well as pathogenic fungi may be found in association with a number of pathologic conditions, and it is frequently difficult to decide whether they are coincidental or the causative factor. This uncertainty arises in chronic suppurative otitis media, in the chronic open wounds following mastoidectomy, and especially in bronchiectatic cavities of the lung. Recently, dissemination of *Candida* and other generally superficial fungi has been observed following intensive use of chemotherapeutic and antibiotic agents.

Aspergillosis is caused by several species of a well known genus which is abundant in nature and is a common laboratory contaminant. In man the infection usually involves the skin, external ear, nose, nasal sinuses, orbit, eye, bronchi, lungs, and occasionally becomes disseminated.

In the paranasal sinuses aspergillosis produces symptoms resembling those of pyogenic infection except for the discharge of pieces of greenish gelatinous membrane in which the organisms can be demonstrated. *Aspergillus* is often present as branching hyphae in sputum of patients with asthma, bronchitis, bronchopneumonia and bronchiectasis, but it is difficult to determine whether it is the causative organism or a secondary invader, especially since it is also identified in patients with pulmonary tuberculosis and malignant tumors. In tissues the abundant mycelial growth is not often associated with fructification, and the chief change is necrosis, although inflammatory cells may be present. A chronic inflammatory reaction with giant cells has been observed in some instances.

Otomycosis in which *Aspergillus* is frequently implicated will be discussed in the section on the ear.

Geotrichosis is an infection due to *Geotrichum*, a yeastlike fungus often found in the mouth and intestinal tract of normal persons. The oral form of the infection clinically resembles thrush. Bronchial geotrichosis, the most frequently recognized form of the infection, can be distinguished from bacterial bronchitis by the character of the sputum which is gelatinous and sometimes blood streaked. The only means of diagnosing geotrichosis is by culture of the organism. Since the infection simulates candidiasis, blastomycosis, cryptococcosis and coccidiomycosis but responds to different therapy, the identification of the fungus is essential.

Mucormycosis is caused by *Mucor* a phycomycete with non-septate hyphae, generally regarded as a saprophyte. It has been found in lesions about the finger nails, and several instances of infection of the orbit and brain have been reported. Gregory, Golden and Haymaker reported 3 cases of mucormycosis in which the portal of entry appeared to be nasal. The fatal infection of the central nervous system by *Mucor* in these cases and of others reported in the literature has been associated with uncontrollable diabetes mellitus.

The mycelia are readily identified as broad, branched filaments without the cross septa usually seen in mycelia of other fungi. In the brain, the mycelia are found in and about blood vessels. There is necrosis of the involved tissues and polymorphonuclear leukocytic exudate.

DEEP INFECTIONS

Several fungi cause deep but focal infections that tend to remain localized. Such infections are considered separately from those that arise in a single, often subclinical lesion, but disseminate, usually with fatal effect, in a small percentage of cases. Examples of deep localized mycoses are maduromycosis, sporotrichosis, chromoblastomycosis, rhinosporidiosis, actinomycosis and nocardiosis. Maduromycosis, in which a variety of fungi is implicated, usually occurs in a lower extremity. Chromoblastomycosis is a verrucous dermal infection also common to the extremities.

Sporotrichosis, caused by *Sporotrichum Schenckii*, occurs in lymph nodes, skin and subcutaneous tissues as nodular lesions that break down to form indolent ulcers. It is of interest to otolaryngologists because of its occurrence in the mucous membranes of nasal and oral cavities and pharynx with involvement of the regional lymph nodes. The fungus can seldom be identified in tissue sections, and since the lesions resemble those of syphilis, tuberculosis, leprosy, and other bacterial and fungus infections, culture is essential in establishing a diagnosis.

Rhinosporidiosis is a mycotic infection of the mucous membranes in various anatomic locations, but it is so outstandingly a nasal infection that it will be considered in the section on the nose.

Actinomycosis is by far the most important of this group, and, in addition, well over half the infections occur in the cervicofacial region. *Actinomyces bovis,* an anaerobic fungus, is found in the so-called normal mouth, in carious teeth, and in deep tonsillar crypts; this would explain the high incidence of the focal lesions in adjacent tissues and in the intestinal tract and, by aspiration, in the lung. A disease of cattle, "lumpy jaw," is almost identical with human cerviofacial actinomycosis and is caused by the same species, but the disease is not transmitted from animal to man.

Cervicofacial actinomycosis usually begins as a hard swelling of the subcutaneous tissues over the mandible. The overlying skin becomes dusky red and small areas of softening appear, which break down and eventually develop into sinuses. Such sinus tracts discharge a watery fluid in which the sulfur granules are seen either grossly or through the low power of the microscope. The process extends very slowly through the subcutaneous tissues, producing additional nodules and sinuses. The underlying bone is not as commonly involved in man as it is in cattle.

Any indolent, long-standing, firm swelling in the neck or about the jaw in which there are multiple sinuses should be looked upon as suggestive of actinomycosis. However, it may be difficult to find the sulfur bodies even after repeated examinations of the secretions.

Under the low power of the microscope the pathognomonic features can be identified. Scattered in usually dense fibrotic tissue are multiple abscesses which consist of collections of polymorphonuclear leukocytes that may be surrounded by larger epithelioid cells, lymphocytes, plasma cells, and fibroblasts. In these abscesses are the typical colonies of the fungus. These consist of a central matted mass of mycelia surrounded by radiating hyphae which are usually characterized by a capsule of gelatinous material. These peripheral hyphae are the clubs or rays.

Infections of the intestine and liver are not uncommon and a more generalized distribution including the bones and lungs occasionally occurs. The large majority of the cervicofacial infections remain localized, but the organisms can be carried to the lungs and viscera by blood-stream dissemination and such infections are practically always fatal.

Nocardiosis, caused by several species of soil-inhabiting, aerobic actinomycetes, may produce subcutaneous lesions indistinguishable from madurmycosis, a pulmonary infection resembling tuberculosis, and a systemic infection, sometimes with metastatic brain lesions. The systemic form of the infection is pyemic and usually originates in the lung. Necrosis of tissue and pus formation are characteristic of the infection in any of its clinical forms. The fungus is made up of branching filaments which may be seen as granules or separate hyphae in abscesses of all sizes. The Gram stain is most effective in demonstrating the branching filaments.

DISSEMINATED FUNGUS INFECTIONS

The fungi responsible for the majority of disseminated infections are *Blastomyces, Histoplasma. Coccidioides* and *Cryptococcus.*

North American blastomycosis, a chronic infection caused by *Blastomyces dermatitidis,* is seen in the United States in a cutaneous and a systemic form. The organism in tissues appears as a round, budding, yeastlike fungus. Cutaneous blastomycosis usually occurs as a primary infection. Although cutaneous and subcutaneous lesions may result from hematogenous spread from a primary lesion in the lung, it is seldom that the systemic form develops in patients with skin lesions of long duration.

The clinical lesion begins as a papule on some exposed part of the body. It enlarges slowly, becomes crusted, and after a long time may become verrucous. Additional lesions develop in the subcutaneous tissues and eventually the process may simulate the nodular, indurated lesion of actinomycosis. However, there is not the definite sinus formation with the serous secretions of the latter, but rather, more ulceration and suppuration. Infections of the larynx are not rare, and such a case with history of mistaken diagnosis is included in the section on the larynx.

Histologically, the reaction is characterized by more or less ulceration of the dermis with striking hyperplasia of the epithelium of the pseudocarcinomatous type. The dermis is infiltrated by tubercle-like granulomas which include giant cells. In addition, there are small intraepidermal and dermal abscesses, a very characteristic feature of the disease.

The budding forms of the fungus are usually seen in giant cells. They are round bodies about the size of the cell nuclei, with thick capsules that can be identified as blastomycetes only by the presence of a single bud springing from the parent cell.

When the infection is disseminated the lungs are always involved, other organs and particularly the bones in some instances. The disseminated infections are practically always fatal.

South American blastomycosis, caused by *Blastomyces brasiliensis,* is not seen in the United States, but the mucocutaneous form presents such serious problems to the rhinolaryngologist that it is included here. The primary lesion may occur on the mucosal surface of the tongue, palate, gums, cheek, lip or nose as a small papule which ulcerates. As the ulcer enlarges the infection invades the subcutaneous tissues. New lesions develop on the mucous membranes until there is extensive involvement, which may ultimately lead to destruction of epiglottis, vocal cords and uvula. The regional lymph nodes become enlarged, and as the mucosal infection becomes more intense the lymph nodes of the neck undergo necrosis and rupture through the skin.

Histologically, the lesions resemble those of the North American disease, and the causative fungus is usually seen in giant cells as a round, thick-walled yeastlike form, distinguished from *B. dermatitidis,* which produces a single bud, only by its multiple budding.

Histoplasmosis in its primary form is a mild pulmonary infection, very often subclinical, produced by *Histoplasma capsulatum.* In less than 1 per cent of cases histoplasmosis occurs in the progressive, usually fatal form, and in at least one-third of these the primary clinical manifestation is in the lips, tongue, ears, pharynx or larynx. There is fever, loss of weight, and usually enlargement of both the liver and the spleen. The fungus has a specific predilection for reticuloendothelium, therefore it is localized particularly in the spleen, lymph nodes, liver and bone marrow, although no tissue is immune. The reaction is a diffuse reticuloendotheliosis rather than a tuberculoid process as seen in other systemic fungus infections. The infection occasionally localizes in the skin and the mucosa. Havens describes as characteristic the appearance of the oral lesions in two of his patients. They were firm and granular and did not bleed when traumatized.

Microscopically, the involved tissue is infiltrated with large mononuclear cells, some packed with the spores. These are small, round, darkly-stained structures surrounded by a clear zone which is the unstained capsule. When bizarre reticuloendothelial cells or Dorothy Reed cells are seen, it is possible that they are evidence of Hodgkin's disease, which frequently has been reported in association with histoplasmosis. The diagnosis of histoplasmosis can usually be made on biopsy material stained by the Gram method or preferably by the periodic acid-Schiff reaction; however, if the spores are not evident, cultures should also be made. Mycelia develop in cultures. No effective treatment for histoplasmosis is known.

Cryptococcosis (torulosis, European blastomycosis) is usually seen as an infection of the brain and meninges, but it may involve the lungs, skin, and other parts. The causative organism, *Cryptococcus neoformans (Torula histolytica),* appears in tissue as a budding fungus. The name European blastomycosis is misleading, for the disease has been reported from many parts of the world including the Pacific islands and North and South America. Cryptococcosis is usually seen in persons between 40 and 60 years of age, although it has been recognized in children under ten, and adults more than 70 years of age. There is no evidence of racial predilection. Cryptococcosis in its disseminated form has a high incidence of association with Hodgkin's disease and other malignant lymphomas or leukemias. It has been suggested that patients with tumors of the reticuloendothelial system have an increased susceptibility to certain infections including cryptococcosis, for the history of the tumor is far more prolonged than that of the infection.

Microscopically, in lesions of skin or mucous membranes a mass of organisms is commonly surrounded by lymphocytes, plasma cells, and numerous giant cells, although the cellular reaction may be lacking. In contrast to blastomycosis the organisms are seen in the skin in the absence of miliary abscesses. Subcutaneous lesions often appear as tumors. In sections, the budding organisms are surrounded by abundant capsular material but occasionally may be seen free within the cytoplasm of giant cells.

Coccidioidomycosis is caused by *Coccidioides immitis.* It has been known to be endemic in the San Joaquin Valley of California for some time, but it is now established that it thrives in the more arid portions of Arizona, New Mexico and Texas. The primary infection is practically always by inhalation so that the initial clinical picture is an acute respiratory infection. Most of these infections regress, but x-ray evidence of lesions in the lungs may remain. In a small percentage of infections there is a general dissemination that pursues a clinical course resembling tuberculosis. This is usually fatal, particularly in Negroes.

Occasionally the primary infection is cutaneous when it may appear in the skin of the face and neck as a chronic ulcerative lesion made up of what appears to be granulation tissue.

Microscopically, the early lesions are essentially purulent, but there may be large mononuclear cells and even giant cells, although the more common reaction is the development of tubercles with a predominance of epithelioid cells and giant cells accompanied by a varying amount of fibrosis and even calcification. The fungus is present practically always as spherules and sporangia, usually in the giant cells. The sporangium is typically large, doubly contoured, and thick-walled and contains many small spores. The diagnosis rests upon the finding of these sporangia. Without the endospores the organism resembles the non-budding spore of *Blastomyces*. Mycelia may be seen in some of the more fulminant lung lesions.

Toxoplasmosis.—Included in the illustrations of fungus diseases in the following plates are several of lesions caused by *Toxoplasma* infections. It must be understood that this organism is a protozoon and *not* a fungus. Its inclusion at this point anticipates the protozoal infections in the next section on tropical diseases.

The life cycle of this organism is not definitely established. Toxoplasmosis is an epizootic of lower animals and birds, but a number of infections in man have been reported since it was first described in 1939.

Clinically it has manifested itself in two forms—a granulomatous encephalitis in infants and an acute generalized disease in adults. It is assumed that infection in infants occurs through the placenta. The mode of infection in adults is not known but may be by insect vector. It is likely there is a relatively high incidence of subclinical infections in adults. In infants there is a severe necrotizing encephalitis, in the debris of which the organisms can be seen, both singly and in characteristic groups. In adults, the principal localization is in the lungs, where the result is interstitial pneumonitis and metaplasia of the alveolar cells in which the organisms can be found. There is also concentration of the organisms in the heart muscle fibers. Recent work by Wilder has shown that chorioretinitis in adults, formerly regarded as tuberculous or nonspecific in origin, is caused by *Toxoplasma* in a large number of cases.

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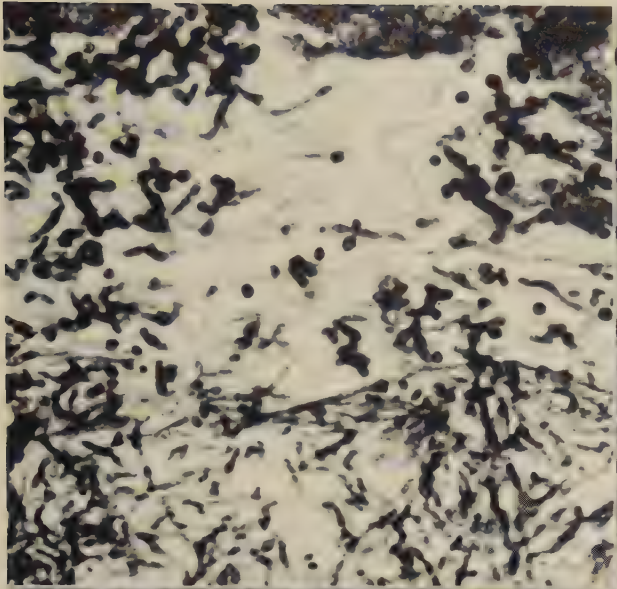
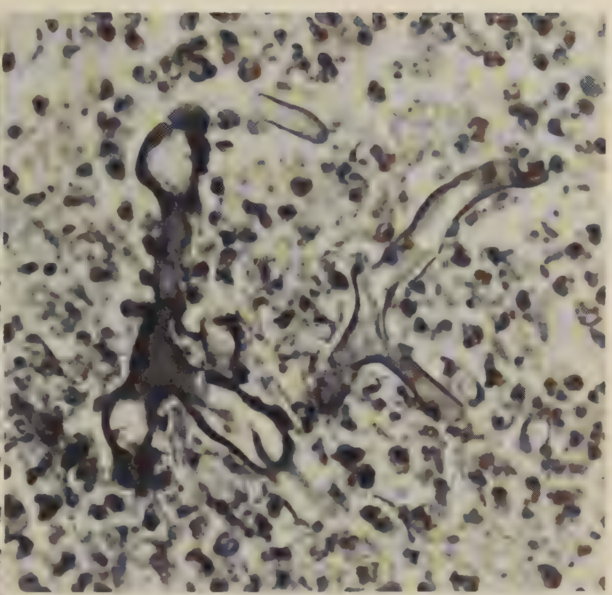
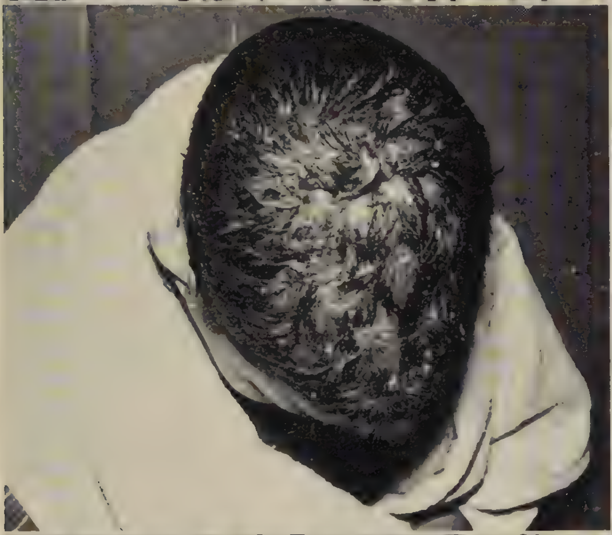




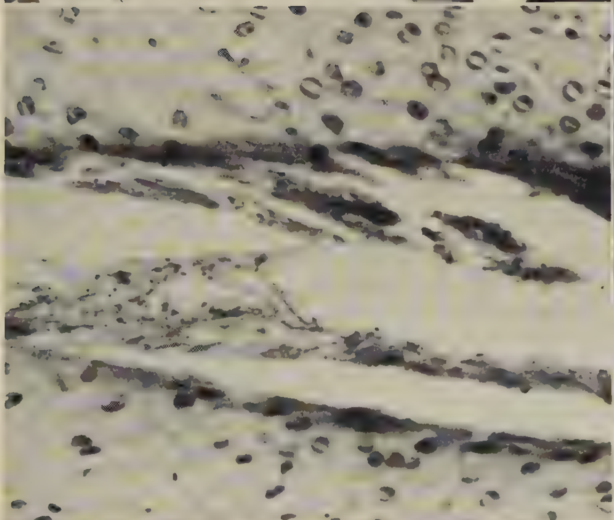


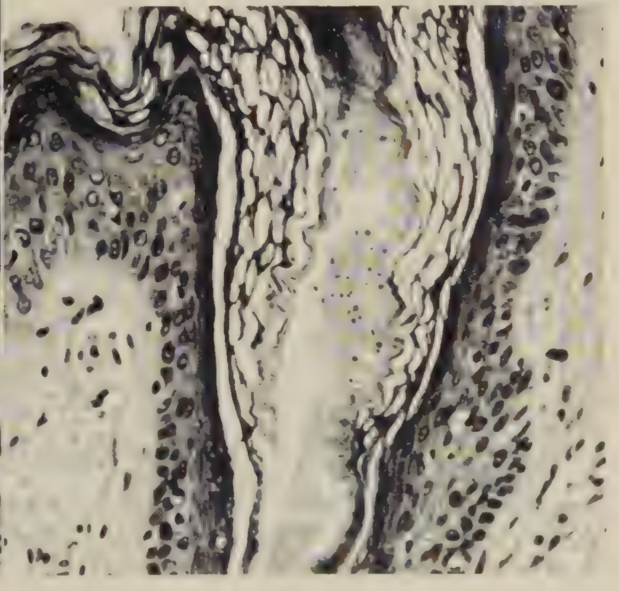
A. Moniliasis (candidiasis), esophagus. Mycelial elements and blastospores abundant in surface tissues. x 450. Bauer stain.

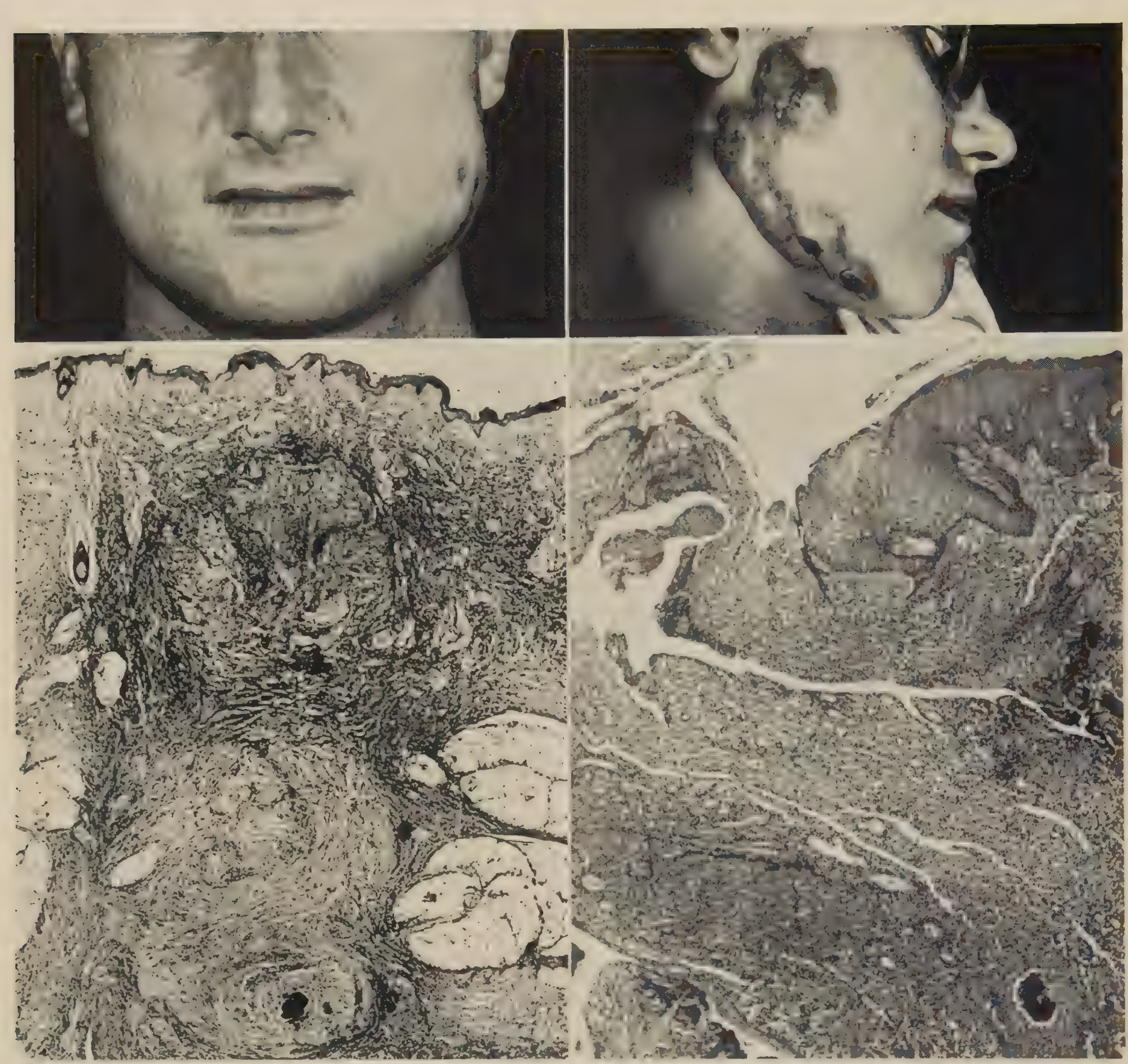
B. Mucormycosis, brain. Very thick, branching, non-septate hyphae with surrounding inflammatory exudate. x 500. Aspergillus and Mucor are widely distributed in nature and usually are harmless saprophytes. They become pathogenic when the resistance of the human or animal host is lowered by malnutrition or intercurrent disease.

C. Tinea favosa (favus), scalp of Arabian boy. Sulfur crusts and the underlying purulent inflammatory reaction of the scalp often result in alopecia. **D.** Hyphae and spores of *Trichophyton schoenleini* in disintegrating hair shaft. x 300.

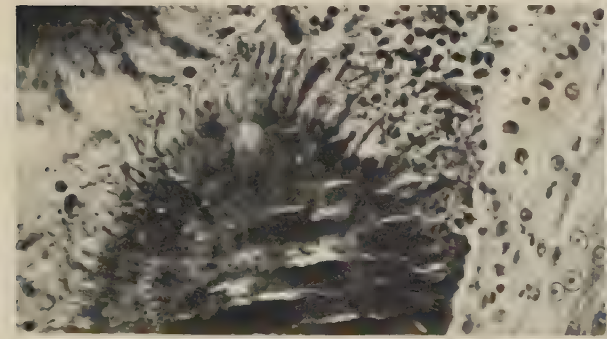
E. Trichophytosis. Spores in hair shaft. x 280. Spores and hyphae may also be found in epidermis outside of shaft.



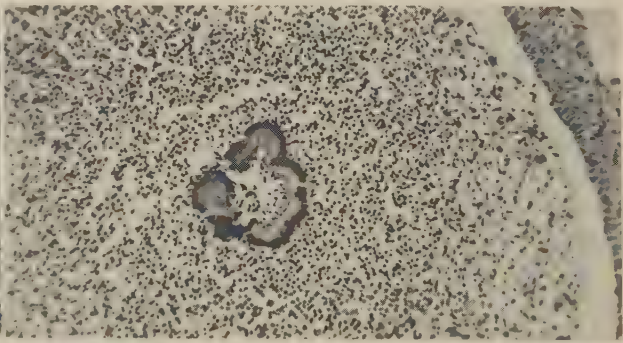




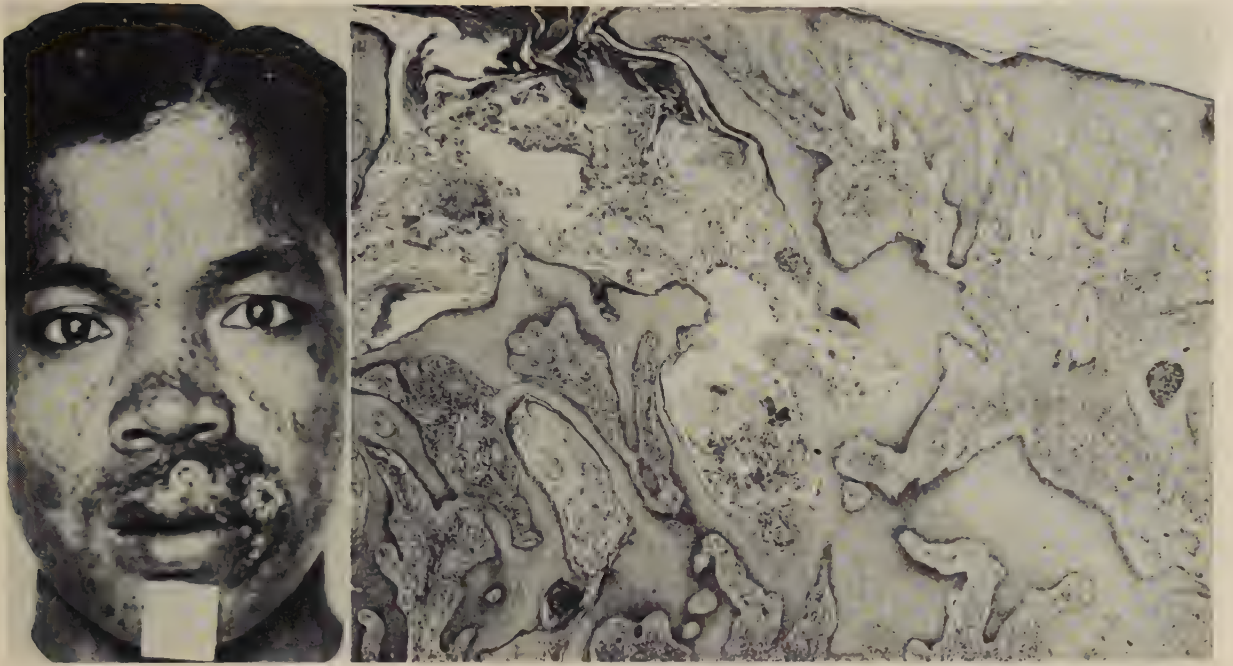
"Lumpy jaw." Cervicofacial region is the common site of actinomycotic infection; typical nodular swelling and multiple sinuses. A. Dermis and subcutaneous tissue show suppurative and granulomatous inflammatory reaction and fibrosis. Abscesses surround the fungus colonies. x 14. B. Sinus in chest wall showing defect in epidermis and very cellular granulation tissue lining the tract. An abscess around colony at bottom. x 48.



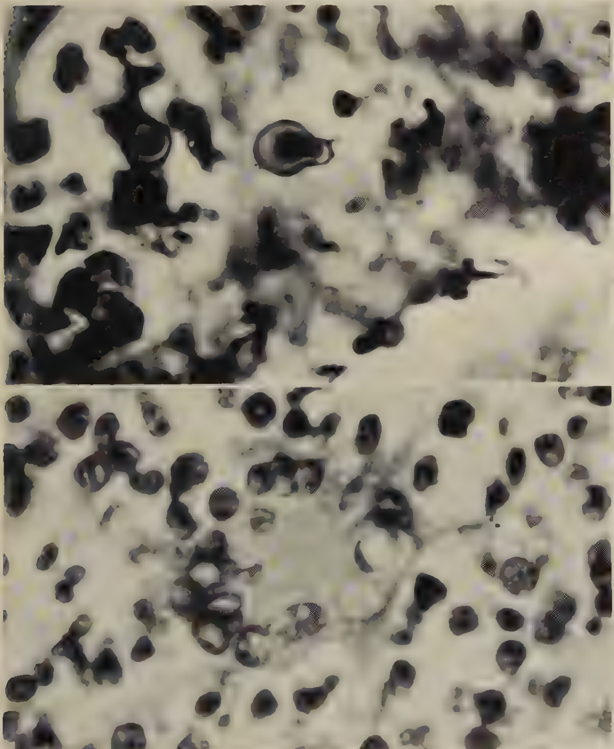
Actinomyces-like colony. The periphery of bacterial colonies (botryomycosis) may be histologically indistinguishable from peripheral clubbing of the actinomycotic granule.



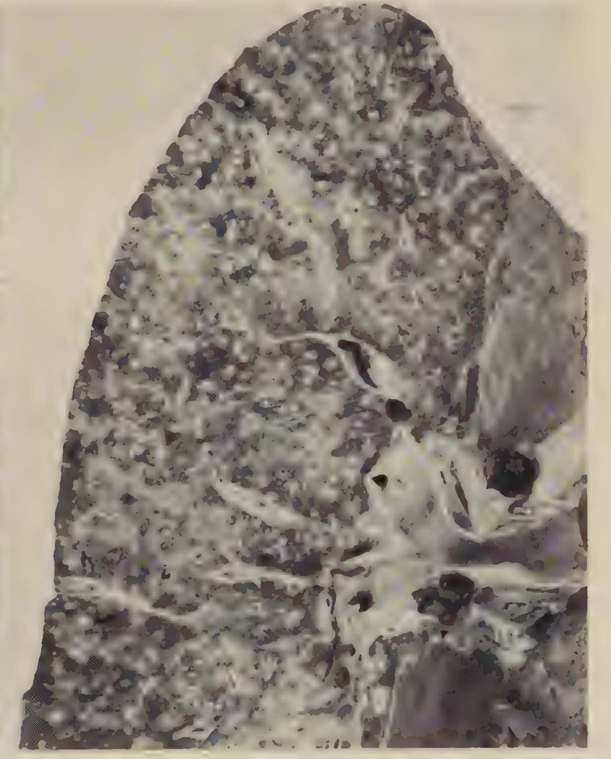
Sulfur granule (clubbed colony of Actinomyces bovis), in typical location, within suppurative inflammatory reaction (abscess) which it provokes. x 100.



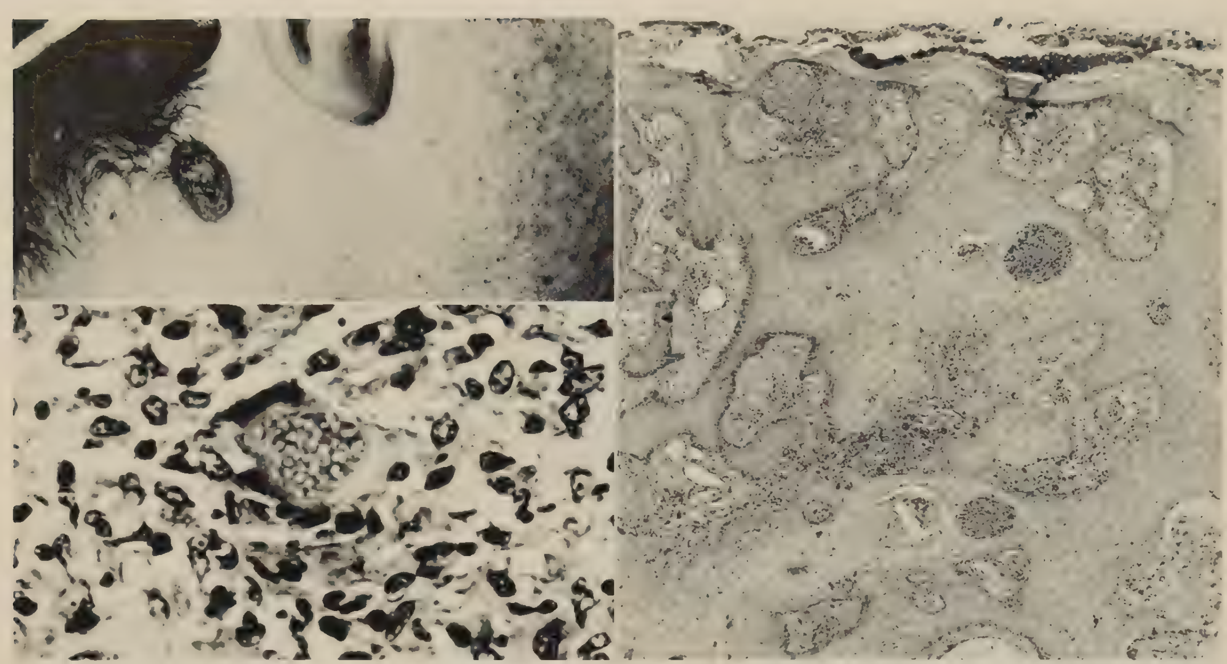
Cutaneous blastomycosis. The two lesions on the upper lip have elevated, spreading peripheral margins. **A.** Typical histologic pattern. Pronounced pseudo-epitheliomatous hyperplasia. Intraepidermal micro-abscesses containing polymorphonuclear leukocytes, and frequently mononuclear cells, eosinophils and organisms. Mixed suppurative and granulomatous reaction in dermis. Organisms may be found within granulomas, in giant cells, or free in the stroma, usually surrounded by polymorphonuclear leukocytes. Eosinophils may be conspicuous. x 18.



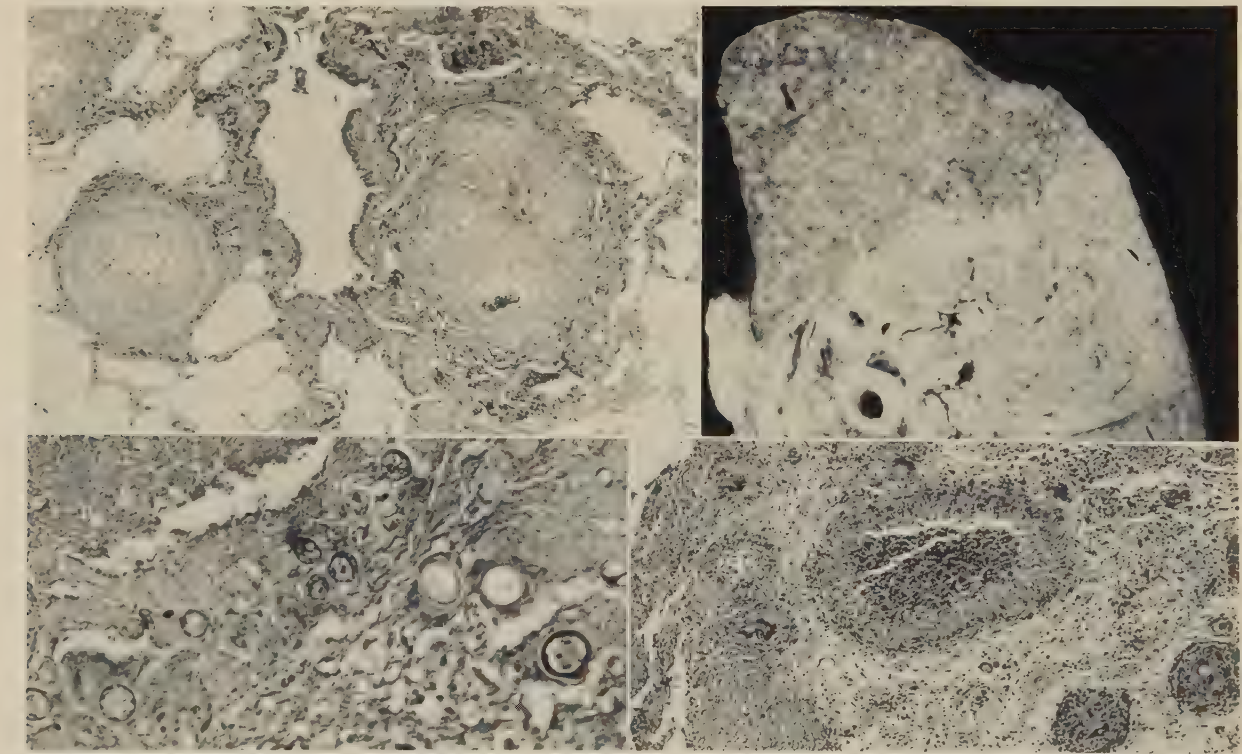
Blastomyces dermatitidis. B. Several organisms including budding forms within an intraepidermal abscess. Laryngeal biopsy specimen. x 1100. **C. Round,** double contoured organism within a giant cell. x 1000. Not endosporulation.



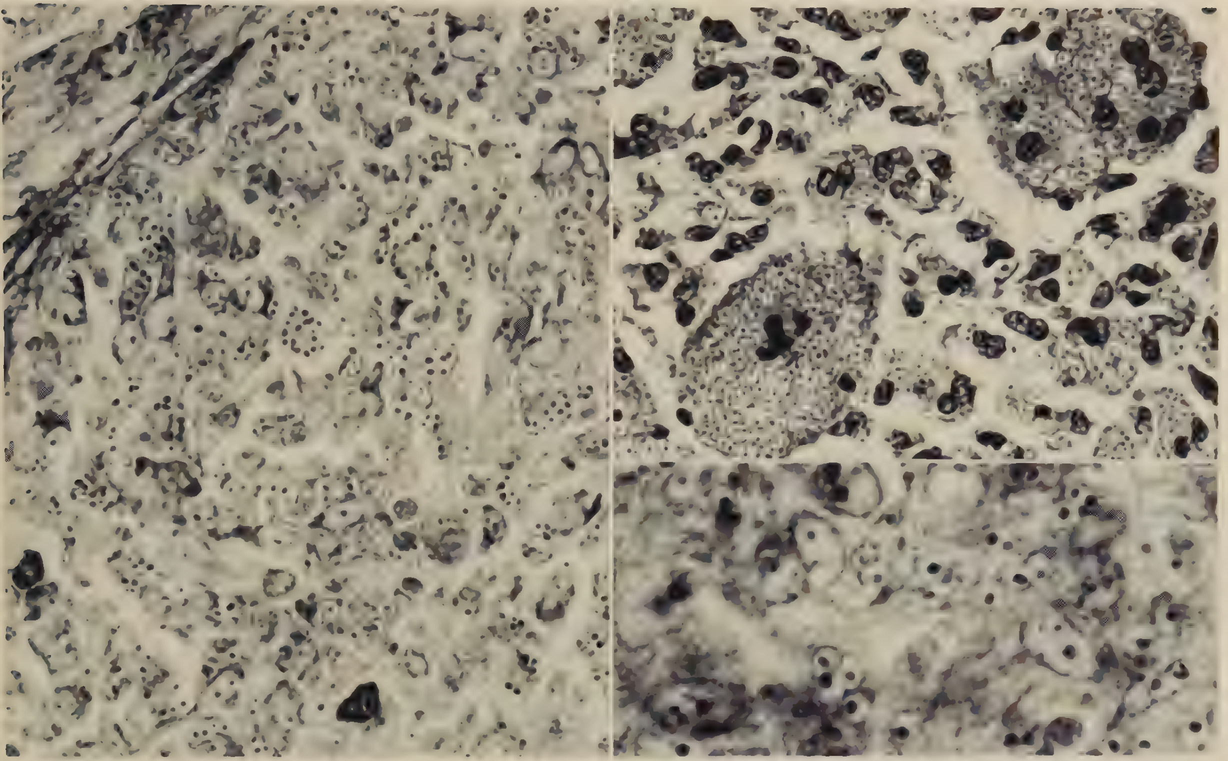
Systemic blastomycosis, lung. In this case, diffuse involvement in the form of small, pale nodules scattered throughout the parenchyma, is grossly indistinguishable from acute miliary tuberculosis.



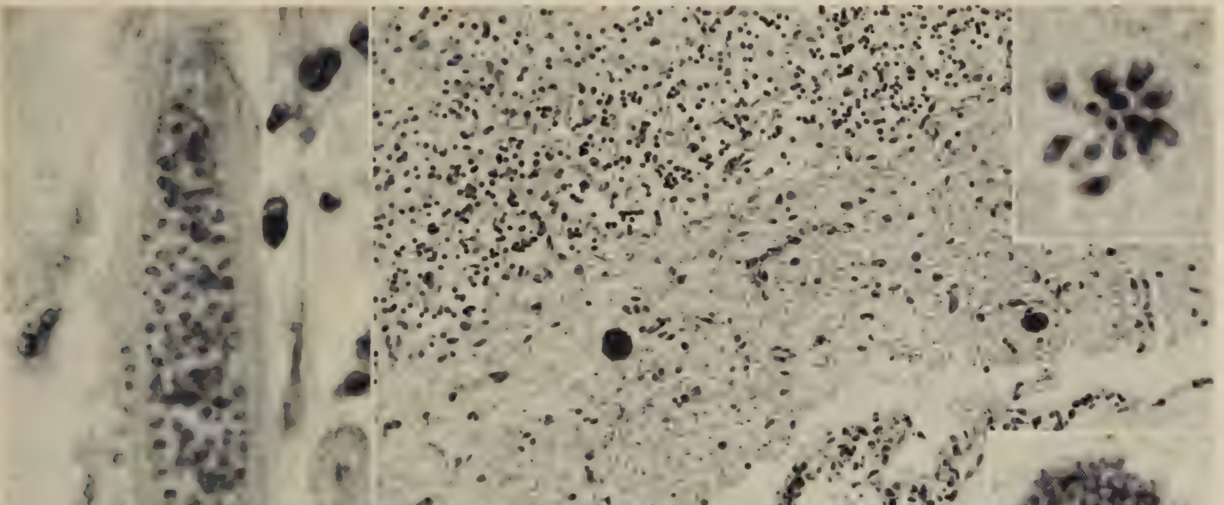
Cutaneous coccidioidomycosis. A. Unusual skin lesion, possibly primary site of infection. **B.** Thick-walled spherule containing endospores in giant cell. Double contoured like Blastomyces, but instead of budding *Coccidioides immitis* produces endospores. x 500. **C.** At low power, histologic picture is indistinguishable from that of blastomycosis-intraepidermal microabscesses, granulomas and pseudoepitheliomatous hyperplasia of the epidermis. x 48.



Pulmonary coccidioidomycosis. D. Healing granulomas resemble those of tuberculosis. x 45. **E.** Lung in case of rapidly fatal primary pulmonary coccidioidomycosis. Confluent abscesses with cavities, necrotizing pneumonia at bottom, discrete nodules at top. **F.** Many spherules in margins of a necrotic lesion. Such non-sporulating organisms may be confused with non-budding forms of blastomycosis. x 220. **G. Sinus tract.** Granulomas in lining tissue contain organisms. The central portion of the large granuloma is composed of polymorphonuclear leukocytes massed about recently expelled endospores. x 62.



Histoplasmosis. When fatal, shows *Histoplasma capsulatum* within reticuloendothelial cells of many organs. **A.** Tongue lesion (biopsy). Proliferating reticuloendothelial cells contain many organisms. x120. **B.** Multiplication of organisms results in enlargement of reticuloendothelial cells of adrenal, x500. **C.** Some variation in size, characteristic clear zone about basophilic central mass. x900.



Toxoplasmosis. D. Toxoplasma in cardiac muscle (dog), a favored site in animal and human infection. **E.** Two pseudocysts in brain (one shown in lower inset, x1000) enlarged by intracellular multiplication of Toxoplasma, x180. The rosette in upper inset (x2000) was found in an adult eye by Wilder, who identified it as a cause of granulomatous chorioretinitis.

CHAPTER 12

TROPICAL DISEASES

Leprosy (Hansen's disease) is not actually a tropical disease, but like other diseases so classed it is more prevalent in the tropics because of the more favorable conditions for its propagation and dissemination. In addition to the tropics there are endemic centers in China, the Scandinavian countries, and the United States. Formerly Wisconsin and Minnesota provided cases, perhaps from among the Scandinavian settlers, but at present leprosy is more common in the Gulf States—surprisingly so to those not familiar with the situation. A better understanding of the disease and increased efforts to recognize it in its early stages are largely responsible for the apparent increased incidence in that part of the country. Because it does occur in this country, it is necessary that the otolaryngologist be cognizant of the early symptoms, especially those about the face and ears, with particular attention to areas of depigmentation, anesthesia, or thickening of the skin.

In spite of the fact that there is no disease in which bacteria are present in such enormous numbers, leprosy is very mildly contagious, and it still is not certain that the *Mycobacterium leprae* is the sole etiologic agent. Numerous attempts at direct human inoculation with the bacterium have been unsuccessful, nor has it been possible until recently to grow it in cultures. It is known that the infection is not hereditary and there has been no evidence so far that the disease is transmitted by animal or insect vectors. There is a natural high immunity to the disease in man, particularly in the adult. This is probably the most important single factor in the low degree of contagiousness. Children during the first few years of life are particularly susceptible, but a prolonged and intimate contact seems to be necessary. It is not uncommon to find several cases in a family.

The disease is the most chronic of the infections. Even when it begins in early life, the patient may live to an old age despite the deformities and reactions that may develop. Death is rarely directly due to the disease, but most commonly results from tuberculosis or the degenerative diseases of old age. The disease is essentially superficial and the lesions are almost entirely confined to the skin, peripheral nerves and lymph nodes, although the organisms themselves are found in all parts of the body, particularly in the liver. The striking deformities that involve the bones of the extremities and face are secondary to the nerve damage.

It is convenient to divide the disease clinically into three forms: the NODULAR OR LEPROMATOUS, the NEURAL OR CLOSED, and the TUBERCULOID. As a matter of fact, there is always nerve involvement, so that the majority of the cases are mixed neural and nodular. There are, however, certain cases in which the skin lesions are limited to macules of depigmentation and anesthesia in which bacteria can not be found. This is the early neural closed and non-contagious form and is the type that leads to the spectacular deformities. In the early stage before the development of nodular lesions, recognition of the disease is very difficult.

In the nodular cases the skin becomes diffusely thickened and nodular, the sites of predilection being the ears, nose, and malar eminences. This is accompanied by alopecia, particularly of the outer portions of the eyebrows. The disease may come to the attention of the otolaryngologist through this distribution of lesions, and the frequency of involvement of the nasal septum and the larynx makes it of great interest to him. Lesions of nasal septum and larynx are discussed under the respective anatomic sites.

A characteristic of the skin nodules of leprosy is that they do not ulcerate except as a result of trauma or during the so-called leprous reaction, a little understood clinical episode of fever, terrific neuritis, and increased activity of the skin lesions. This may last from a few hours to months.

The tuberculoid form is very likely a hyperergic reaction. It is characterized by a circumscribed nodular lesion, usually on the face, that expands peripherally leaving a healed center. It tends to regress spontaneously, something that the nodules in lepromatous leprosy do not do. Histologically it differs from the nodular lesions in that it is largely a tubercle reaction and organisms are absent. It is apparently evidence of high immunity and, like the closed lesion, it is not contagious.

Microscopically, the nodular lesions are characterized by diffuse infiltration by the foamy lepra cells containing great numbers of bacteria. The overlying epidermis may be atrophic or hyperkeratotic. The regional lymph nodes are always involved. They are not much enlarged, but histologically they show diffuse infiltration with lepra cells. One of the surest means of obtaining diagnostic smears is by aspiration of a lymph node. This is much more certain than depending on a smear from the nasal septum.

In the early involvement of the nerve, bacteria and lepra cells infiltrate between the nerve fibrils. In the course of time these are replacd by dense fibrosis which eventually converts the nerve into a nodular fibrous cord. The common involvement of the posterior auricular nerve affords one of the diagnostic features of the disease and is readily available for recognition by the otologist.

Considerable progress in the treatment of leprosy has been made with chemotherapy, especially with the sulfones.

Yaws is of little importance in this country, but it offers a problem to the otolaryngologist because of the frequent involvement of the mucocutaneous junctions by the frambesiform lesions and, in a later stage of the disease, mutilating ulceration of the nose called GANGOSA (rhinopharyngitis mutilans). This stage of yaws corresponds somewhat to the tertiary gummatous stage of syphilis. The lesion usually begins as a small nodule in the nose or on the palate. Proceeding from this focus there is rapid destruction of tissue, at times to the extent that the orbit and the cavities of the nose and pharynx are seen as a single space.

Another clinical entity is GOUNDOU which consists of a protruding exostosis of the superior maxilla and the nasal bones. It is not definitely established, however, that this osseous change is always due to yaws.

Yaws is one of the three tropical diseases caused by *Treponema,* the other two being pinta, endemic in the South American countries and Africa, and bejel which is restricted to the Valley of the Euphrates. All of these diseases have much in common with syphilis, the fourth of the human treponematoses and the only one of the four that is a venereal disease. Yaws is strictly a tropical disease which occurs rarely, if ever, in the white race. It is particularly common in childhood.

The primary lesion usually occurs on the lower extremities and is called the "mother yaw." It differs little from the later skin lesions except that it is larger and is always ulcerated. The typical eruption is made up of raspberry-like lesions that are particularly common about the mouth, nares, and other mucocutaneous junctions. This stage is self-limiting and usually disappears within a year, leaving little residual evidence. The tertiary form includes gangosa and gummatous lesions of bones and subcutaneous tissues that leave marked deformities.

Histologically, the secondary lesion is characterized by hyperkeratosis with marked elongation of the rete pegs. There is edema of the epidermis, the papillae are congested, and the vascular endothelium is swollen, but it is not the aggressive inflammatory process seen in syphilis. *Treponema* can be demonstrated in both the papillae of the dermis and the basal layer of the epidermis. The disease is readily controlled by the salvarsan group of drugs and by penicillin.

Smallpox is an acute contagious exanthem caused by a specific virus that has a particular affinity for the skin. It is not necessary to go into the clinical aspects of this disease, but simply to call attention to the possibilities of involvement of the mucosae, especially of the mouth, pharynx and esophagus, and of the frequency of such complications as laryngitis and otitis media.

The pox is one of the vesicular dermatoses beginning in the upper cells of the malphighian layer. These undergo a colliquative necrosis which the dermatologist speaks of as ballooning degeneration. The cells swell to enormous size and leave a reticular net work in the resulting vesicle. The vesicle later becomes infiltrated with polymorphonuclear leukocytes, the pustular stage clinically, and there is then extension of the purulent reaction into the dermis. It is this feature that results in scarring.

Intranuclear inclusions may be found in the affected prickle cells and the more striking intracytoplasmic Guarnieri bodies, which may be either acidophilic or basophilic.

Rickettsial Diseases.—The *Rickettsiae* are between the viruses and the bacteria in the biologic scale. Like the bacteria they can be seen under the microscope, but like the viruses they will pass through certain filters and are obligatory tissue dwellers and thus cannot be cultivated on artificial media but can be grown on chick embryo. With the exception of the Q fevers, the *Rickettsiae* that are pathogenic to man are endothelial invaders. The pathology, therefore, has the common denominator of vasculitis. The diseases differ clinically and pathologically to a minor degree in the distribution and severity of the lesions.

The **typhus-fever** group includes the louse-borne EPIDEMIC TYPHUS, the rat-flea-borne MURINE TYPHUS, and BRILL'S DISEASE, a mild recurrent form of typhus. The last two are endemic in this country, the murine fever being fairly common along the coast, particularly in the Southern States.

The second group are the **scrub typhus,** or mite-borne diseases, not of concern to us here. The third and most important to us in this country is the **spotted-fever** group, transmitted by the wood tick and dog tick. Spotted fever was originally endemic in Montana but has since been reported in practically every state in the Union.

The reason for including these diseases is that occasionally Rocky Mountain spotted fever exhibits a primary lesion at the site of the tick bite as does scrub typhus in practically every case. This bite may be so located that it comes to the attention of the otolaryngologist. It will not be necessary to go into the clinical details of each of the diseases, for, with the exception of murine typhus and Brill's disease, they are usually so fulminant that it is not likely that even the initial symptoms would bring the patient first to the otolaryngologist. The vascular lesions, however, localizing in the tongue, pharyngeal and oral tissues might bring the otolaryngologist into consultation.

The rash of Rocky Mountain spotted fever begins characteristically on the hands and feet and spreads to the rest of the body. In epidemic typhus fever the rash is usually limited to the trunk. The Weil-Felix agglutination test with the various strains of proteus bacillus are available, as well as complement fixation tests, for differentiation. The recent discovery of the effectiveness of chloromycetin and aureomycin in the treatment of rickettsial diseases has altered the prognosis considerably.

Plague is an acute febrile disease characterized by buboes, septicemia, petechial and diffuse hemorrhages into the skin and serous and mucosal surfaces. These are the usual manifestations, but in certain regions, particularly in China, the epidemic form is pneumonic. Rodents are the natural reservoir, rats the most important, but in California the ground squirrel is a serious menance. The disease is due to the *Pasteurella pestis* and is transmitted to man by the bite of the rat flea.

Clinically, the bubonic form is not quite so fulminant and the mortality rate is somewhat lower than those of the septicemic and pneumonic forms which are always fatal. The onset is sudden—a chill, steeply rising temperature, rapid pulse and respiration. There is severe leukocytosis that may reach 40,000. The blood culture is positive in about fifty per cent of the cases. The bubo, which may be single or multiple, develops on the second to the fifth day. It may reach the size of an egg and it is very painful and tender. The inguinal nodes are involved in about seventy-five per cent of the cases, but the axillary and cervical nodes are involved less frequently. The tonsil was the site of such a lesion in one Registry case.

In fatal cases there is not the sharp differentiation of the three clinical types because there is always a terminal septicemia and the lungs are practically always involved.

The histologic picture is characterized by hemorrhage and necrosis. The organisms are present in great numbers and their powerful toxin destroys the vascular endothelium. The process is so fulminant that there is little cellular exudate. The hemorrhage, necrosis, and edema extend beyond the limits of the involved lymph node. There is no other disease that gives the characteristic picture of hemorrhage, edema, necrosis, and abundant bacteria.

Anthrax (Malignant pustule – woolsorters' disease) results from infection of abraded skin by the *Bacillus anthracis*. This may occur on the face, but not so commonly now as formerly when infections were incurred from shaving brushes. Lesions of the head and neck may result from the practice of carrying hides over the shoulder.

At the site of infection a papule develops and is surrounded by a zone of hyperemia. The papule later becomes vesicular and ruptures, forming a black eschar which is the characteristic clinical feature. Satellite vesicles appear and the lesion may become several centimeters in diameter. There is usually adenitis of the regional lymph nodes. The infection can remain localized and heal spontaneously, but septicemia is the dangerous possibility, particularly if the initial lesion is a cellulitis instead of a restricted papule. The diagnosis of the lesion is comparatively simple because it contains great numbers of bacteria that may be identified by smear and culture.

The organism is usually of highly virulent nature and the reaction is one of liquefaction necrosis rather than exudation. The exudate is predominantly serofibrinous, more or less hemorrhagic, but with comparatively few cells of exudate. Large numbers of the typically rod-shaped, sporulating organisms are present in the tissues. The blood vessels are dilated and collagen fibrils necrotic. The process extends through the dermis into the subcutaneous tissue.

PARASITIC INFECTIONS

Cutaneous leishmaniasis is a chronic granulomatous lesion of the skin due to infection by several species of *Leishmania*, especially *L. tropica* and *L. braziliensis*. It is most common on an exposed surface, particularly on the face, and is often seen on the ears of chicle gatherers in South American countries. The lesion is usually single but may be multiple. The variety of clinical names is based largely on geography, for example, Delhi boil and Oriental sore. Clinically, the disease manifests itself as a chronic boil-like papule which may undergo ulceration, but characteristically it is sharply defined with somewhat rolled edges. There is usually a history of a bug bite.

The more serious type of skin involvement is seen in South America through infection of the mucocutaneous junctions. Lymphatic spread from a single cutaneous boil may account for extensive involvement. Usually the initial papule is on the anterior part of the nasal septum, and rapid spread complicated by secondary infection results in destruction of much tissue in the nose, cheek, mouth, pharynx, and even larynx. There is eventually spontaneous healing but with much disfiguring scarring. This form of the disease is called espundia. A rare manifestation is the development of a nasal polyp that is complicated by destruction of nasal tissue. Costa described such a case.

The uncomplicated boil shows a diffuse infiltration of the dermis by histiocytes which contain great numbers of organisms. The *Leishmania* as it occurs in tissues may look a great deal like *Histoplasma* and care must be taken to differentiate the two organisms. The *Leishmania* is identified by the two nuclei, the round trophic nucleus, and the closely associated, somewhat elongated kinetoplast.

The reaction in its earlier stages is in the upper portion of the dermis but spreads later to the subcutaneous fat. The epidermis is not directly infected but undergoes secondary necrosis from pressure and interference with its blood supply. Tubercles may appear as collections of histiocytes palisaded about a necrotic focus. There may even be Langhans giant cells.

The basic picture in espundia is the same except that it is complicated by a secondary purulent inflammatory reaction and granulation tissue.

HELMINTHS

Trichinosis is a serious problem in the United States where its incidence is estimated at 15 per cent of the population. The natural host of the adult nematode, *Trichinella spiralis,* is the pig. The helminth in its larval form is transmitted to man by the ingestion of pork cooked insufficiently to kill the larvae encysted in the muscles. In the human intestinal tract the larvae are released during the process of digestion and anchor themselves to the mucosa of the small intestine where they reach maturity in a few days. After a time the mature female deposits larvae in the intestinal lymphatics from which large numbers reach the blood stream and are distributed to all organs and tissues. They are capable of attaining full development, however, only within the skeletal muscle fibers. In about five weeks they reach this stage and become encapsulated. They can remain dormant but in an infectious state for many years. The muscles most commonly involved are the diaphragm, intercostals, ocular and masseter groups, but those of the pharynx, particularly of the tonsillar capsule, and those of the larynx are occasionally invaded.

The symptoms depend upon the intensity of the infection and the muscles involved. There may be an active febrile state, intestinal upset, pains in the involved parts, and blood eosinophilia. The diagnosis can sometimes be made by biopsy from the skeletal muscles, such as the deltoid or those of the calf.

Microscopically, the invaded muscle fiber is enlarged and takes a basophilic stain; the coiled larva in a capsule is the diagnostic feature. There is usually active interstitial myositis which in the later stages is predominantly eosinophilic. It is possible to find collections of eosinophils at some distance from the affected fiber. Such collections can be interpreted as at least very suggestive of trichinosis even if the parasite cannot be demonstrated. Many of the larvae die and become calcified, stimulating a foreign body reaction.

In the section on the pharynx is an illustration of the parasite in the pharyngeal muscle of a 56-year-old man who died of carcinoma of the lip. There was no record of symptoms incident to trichinosis.

Onchocerciasis is infection of the skin by *Onchocerca volvulus,* one of the filarial worms. It is the only filaria that localizes in the skin and subcutaneous tissues. No microfilariae are released into the blood stream as are those of other species. The disease is common in Mexico, Guatemala, and West Africa, depending on the habitat of the transmitting insect, the buffalo gnat (Simulium). It is particularly prevalent among natives working on coffee and tea plantations. In Central Americans it is manifested by the development of subcutaneous lumps, particularly in the scalp, which may be mistaken for sebaceous cysts. For some reason these lesions are more common on the trunk in the African endemic centers. The nodules develop in response to the localization of the adult worms.

Great numbers of the microfilariae migrate from the nodules into the neighboring tissues including the epidermis where they can be readily found on microscopic examination. The microfilariae themselves cause little reaction except when they invade the eye, but onchocerciasis is the commonest cause of blindness in the endemic centers.

Histologically, the nodule is made up of a twisted mass of adult worms embedded in chronic inflammatory tissue which may also contain foci of acute inflammation; in the late stages it may become completely fibrotic.

Several other species of helminths are of minor importance in the United States. One is the trematode, *Paragonimus westermani,* the lung fluke, that may come to the attention of the chest surgeon as a diagnostic problem, or the neurosurgeon when it invades the brain. This worm is endemic in the Far East where the infection is acquired by eating raw crab meat. The hermaphroditic adult, when it reaches maturity in the lung, produces a clinical syndrome of persistent cough accompanied by bloody sputum. The diagnosis is established by identifying the ova in the sputum. Bronchiectasis or lung abscess usually complicates the picture. The young worms may migrate through the soft tissues until they reach the brain, or the ova may be disseminated by the blood stream. The resulting reaction may produce serious or fatal lesions of the central nervous system. The following illustrations include one of the adult worm in its subpleural cyst and another showing ova in the brain.

Dissemination of ova may complicate other worm infections. The ova of *Schistosoma* are found in scattered regions remote from the adult worm–lymph nodes and brain, for example. Even with infections by the relatively inert *Ascaris* serious complications can result, especially lung lesions, from the lodgement of larvae or ova. Examples are included in the illustrations.

MYIASIS

Infestation of tissue by fly larvae is more common in the tropics but may occur in other climates. Three types of Diptera are implicated; one, the obligate, which is specifically parasitic to man. The best example is *Dermatobia hominis,* the larva of which buries itself in subcutaneous tissue after it has been deposited on the skin by its vector host, the female mosquito, *Janthinosoma lutzi*. It is a tropical parasite. The semiobligate, such as the *Chrysomiae,* requires an animal host but not necessarily man. The accidentally parasitic are not necessarily parasitic but deposit their larvae in any convenient and favorable portion of the body, including the orifices, or on exposed necrotic tissue. These include the screw worm *Cochliomyia.*

The *Chrysomiae* are present in the United States. While they usually deposit their ova in the wounds of cattle and other domestic animals, they are occasionally attracted to human beings, particularly if they emit odors from sinusitis or ozena. The ova are most commonly deposited in the nose. The resulting larvae are aggressive invaders and may cause great destruction to the nose, palate, and pharynx.

There may be incidental infections in the ear and nose by larvae of less destructive species as the *Muscidae,* including the common house fly, and *Sarcophaga,* the blue bottle fly. These larvae usually remain in necrotic tissue rather than penetrating healthy tissue.

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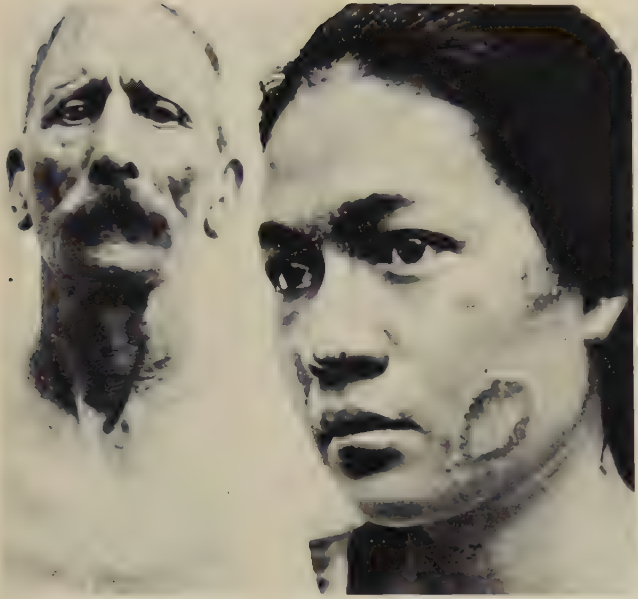
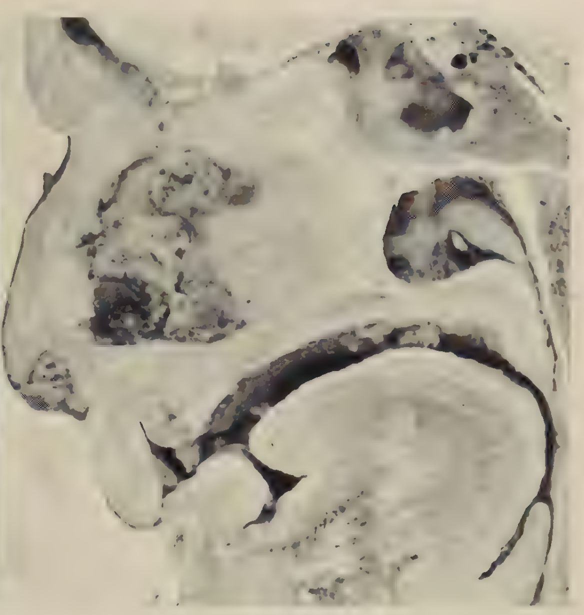
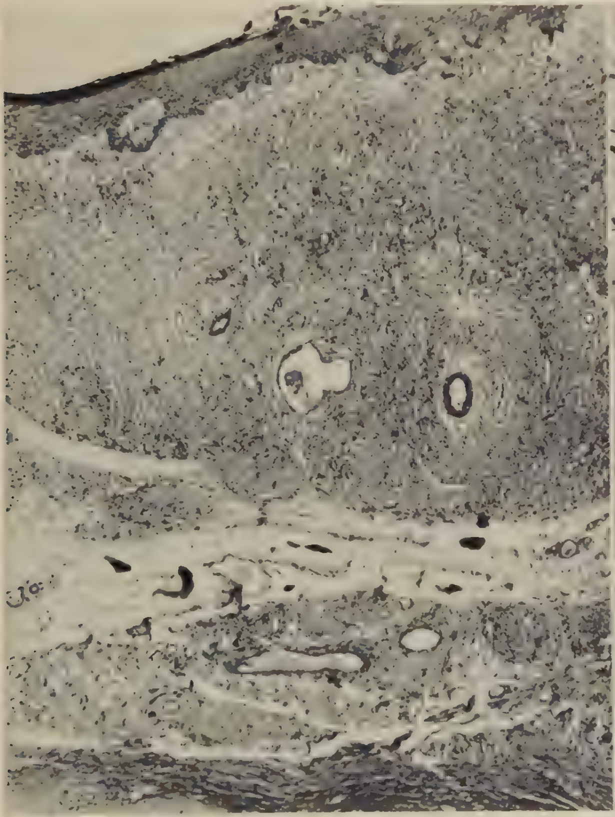


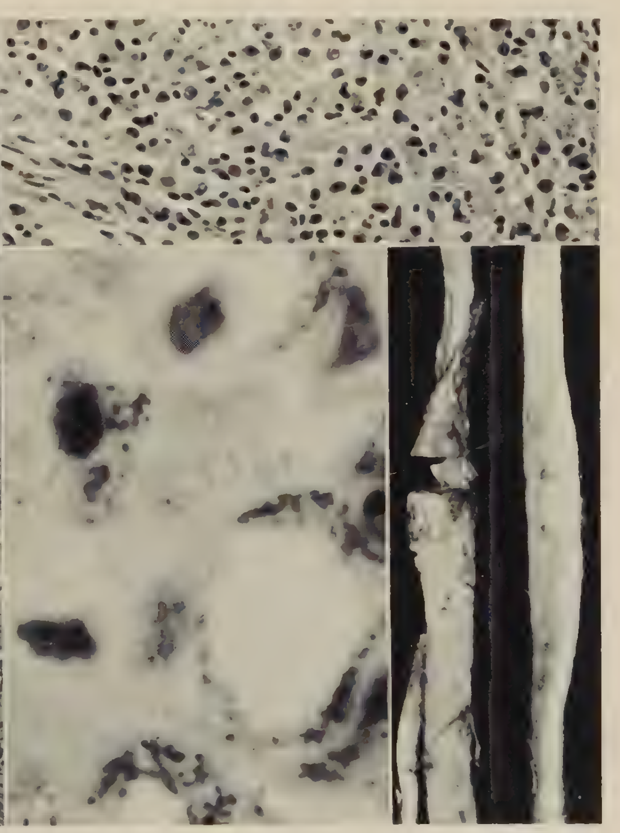
Two clinical types: **A. Lepromatous leprosy.** Nodular or diffuse cutaneous infiltrations which contain numerous organisms. Eyebrows partially gone. **B. Tuberculoid leprosy.** Large anesthetic macule with depressed central area and erythematous margins. Tubercle-like granulomas in dermis and peripheral nerves, but no bacilli.



Upper respiratory tract in advanced case of lepromatous leprosy. Sectioned head shows destruction of large part of nasal septum. Extensive pharyngeal infiltrations, with adhesions of soft palate to pharyngeal wall.

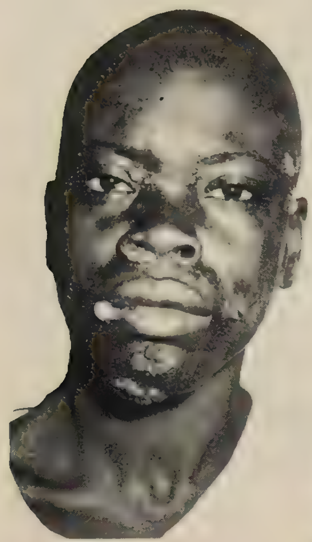


Nasal mucous membrane. Septal mucosa is greatly thickened to perichondrium, by diffuse infiltrations of lepra cells.

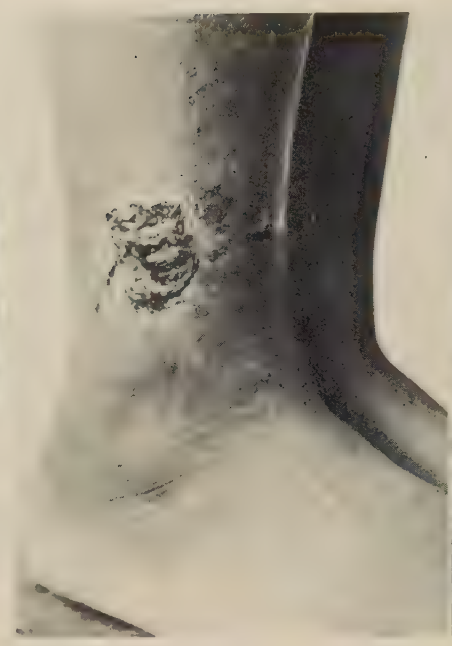


C. Lepra cells. Hyperplastic foamy histiocytes. **D.** ***M. leprae*** within lepra cells. x 1000. **E. Nerves in tuberculoid leprosy.** Thickenings of ulnar and occipital nerves.

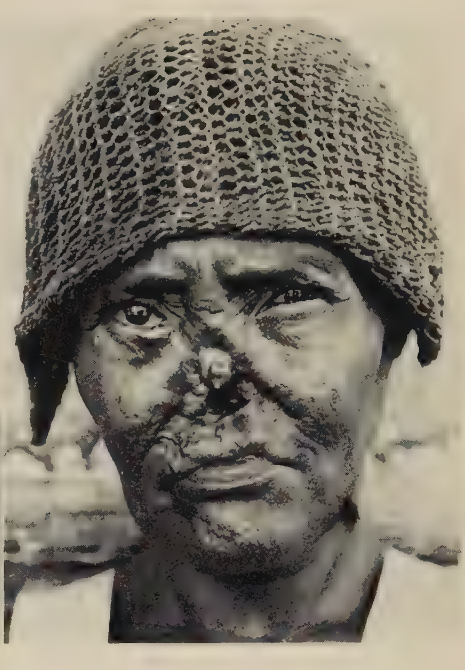
YAWS



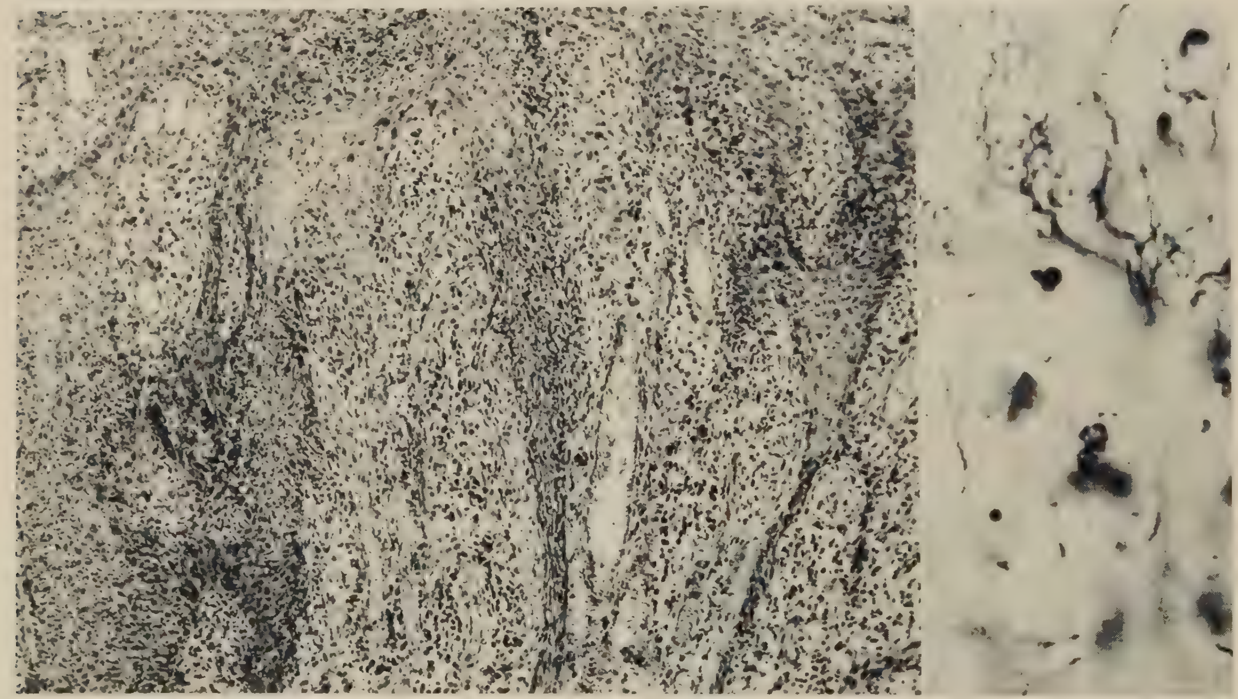
A. Secondary lesions (frambesiform) develop anywhere on the skin, but commonly at mucocutaneous junctions. Typically an elevated nodule with verrucous raspberry-like surface, 1 to 2 cm. in diameter.



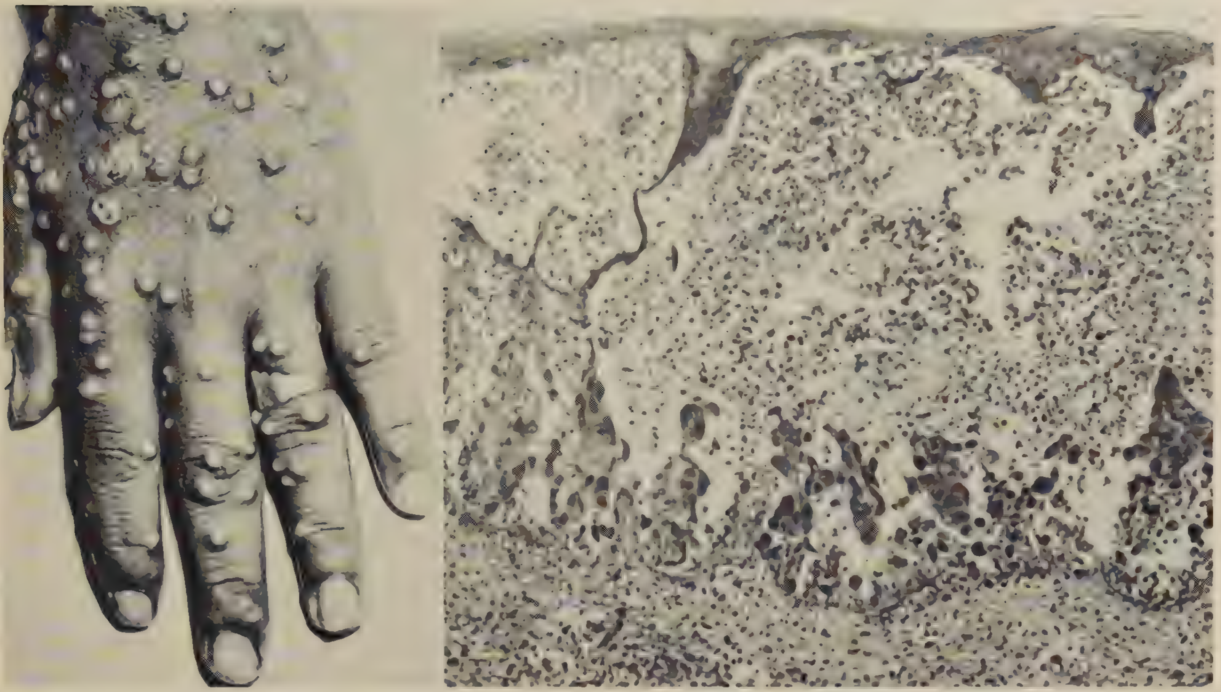
B. The primary or mother yaw, most commonly seen on the leg, is a crusted, elevated irregular lesion, larger and more ulcerative than the secondary lesion.



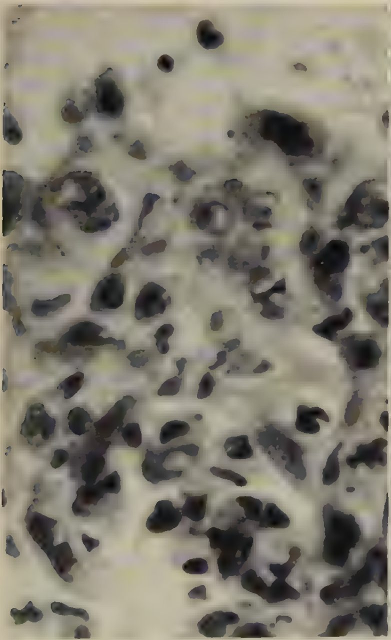
C. Gangosa (rhinopharyngitis mutilans) is a tertiary gummatous stage that involves cartilage and bone as well as skin. Gummas develop in bones and soft tissues elsewhere and result in marked deformities.



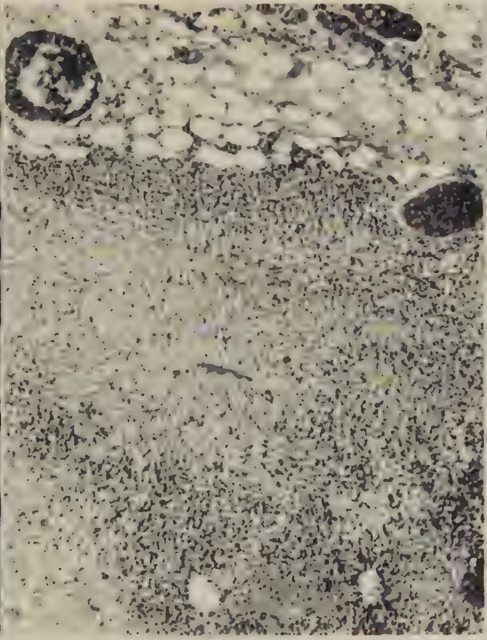
D. Histologic features of primary lesion. Crusted, ulcerated, secondarily infected surface; marked elongation of rete pegs; edema; dense infiltration of dermis and epidermis by leukocytes and plasma cells; small abscesses and dilatation of superficial blood vessels are features of both primary and secondary lesions, but all are more prominent in the mother yaw. x 100. **E.** *Treponema pertenue,* morphologically identical with *Treponema pallidum,* predominantly in epidermis, but also in dermal papillae. x 1360.



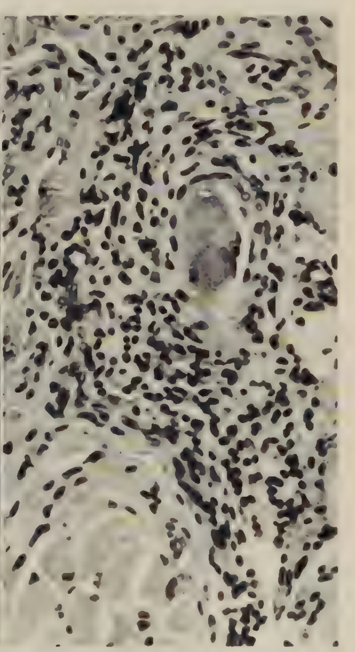
Smallpox, ninth day of eruption. **A.** Pustules, discrete in this case, are typically umbilicated before they ulcerate. Mucous membranes of the lips, mouth, nose, pharynx, larynx and esophagus may be involved but instead of vesicles and postules, often present eroded, reddened, ulcerated lesions. **B.** The serum and fibrinous content of the vesicles are obscured by purulent exudate. The multiloculated vesicle within the malpighian layer is formed by two types of degenerative changes in the epithelial cells; "reticular colliquation" of upper layers and "ballooning degeneration" of lower cells. Scarring results from involvement of the dermis. x 160.



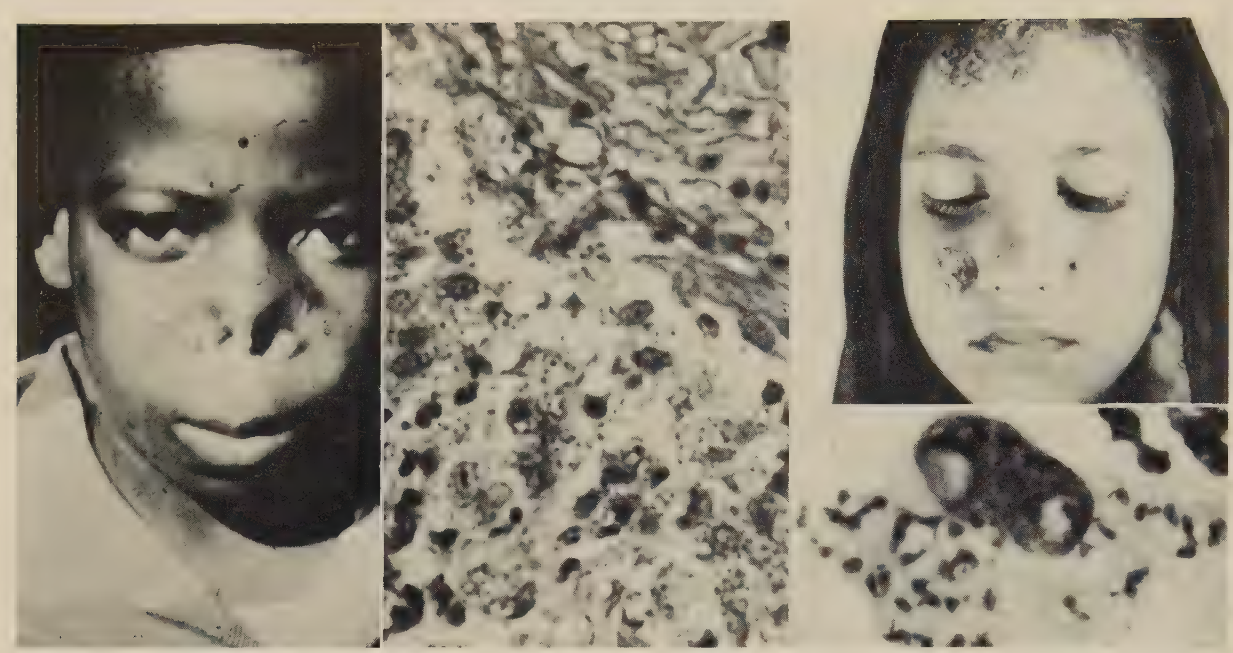
Guarnieri bodies. Intracytoplasmic inclusion bodies within epithelial cells in smallpox, composed of tiny elementary bodies, the Paschen bodies, now accepted as the cause of the disease. x 640.



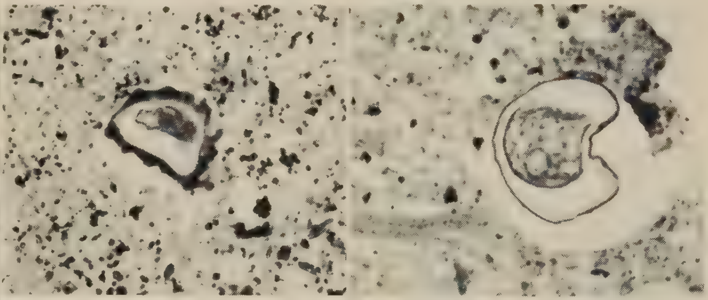
Plague. Tonsil, hemorrhagic and necrotic. x 75. A fulminant infection (bubonic, pneumonic and septicemic) with similar changes in spleen and lymph nodes. Causal organism, *Pasteurella pestis,* transmitted usually by fleas from a varied animal reservoir.



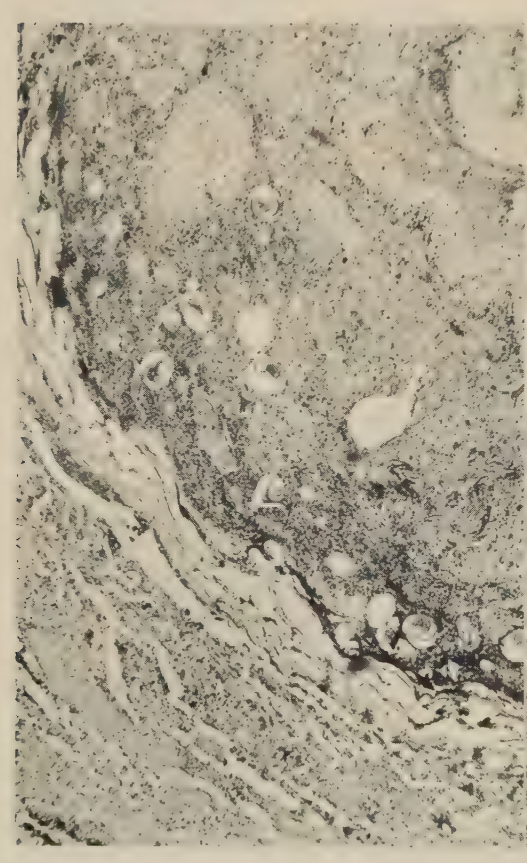
Epidemic typhus, tongue. Lymphocytes, plasma cells, and macrophages about partially necrotic thrombosed arteriole–the "typhus nodule." x 250.



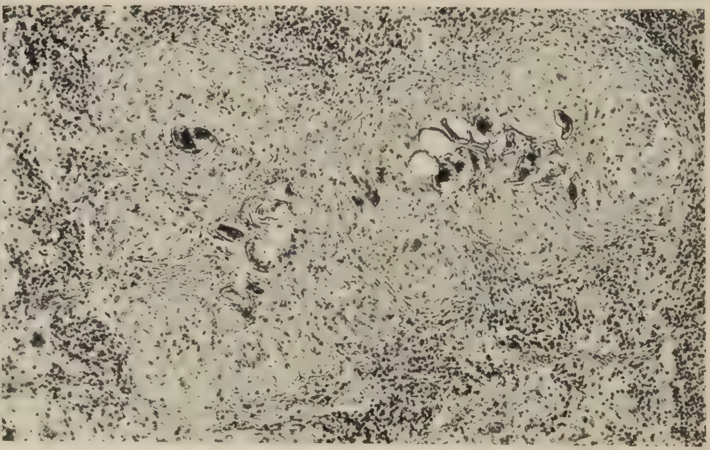
Leishmaniasis. The dermal form may involve the mucocutaneous junctions and result in great deformity. A. Espundia of South America. B. Dermal lesions in an Egyptian. C. Tissues infiltrated with histiocytes containing *Leishmania tropica,* seen in detail in D. x 1000. At low magnification the organism may be confused with histoplasma.



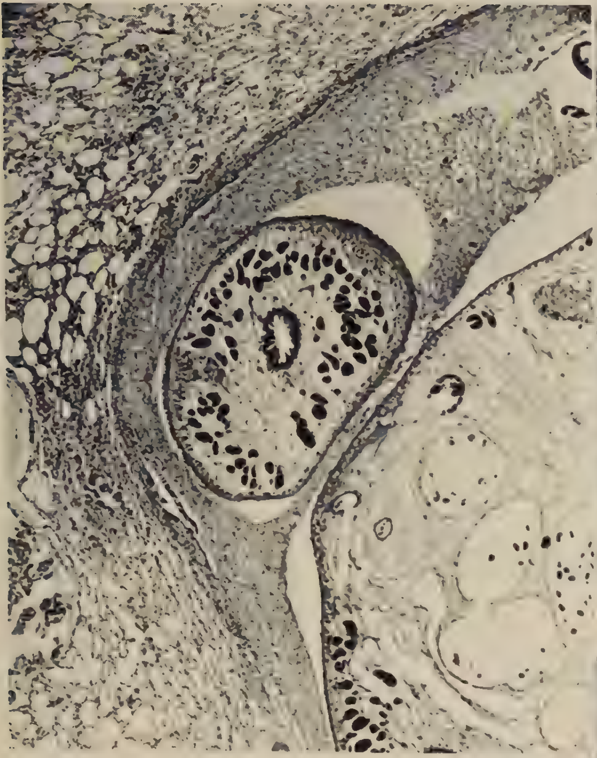
Left, Ascaris ovum with characteristic thick irregular sheath. x 350. Right, Ascaris ovum without sheath. x 430.



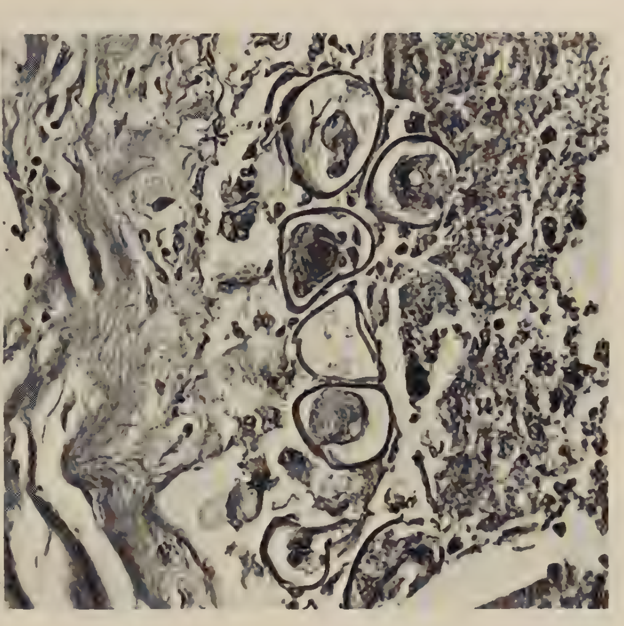
Ascariasis. Ascaris abscess, lung. Ova in periphery. Ascariasis is generally a relatively harmless intestinal infection, unless ova reach the lung.



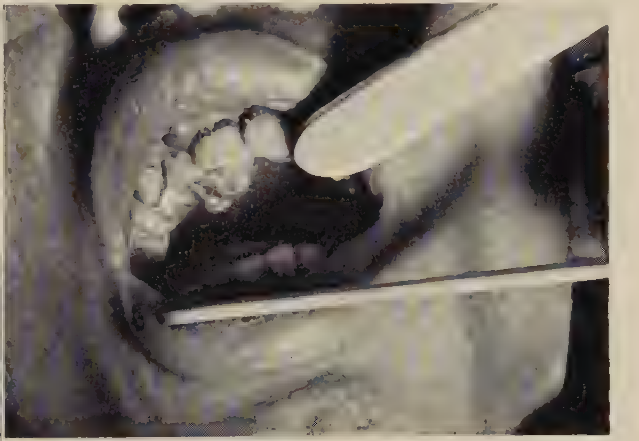
Shistosomiasis, brain. Granuloma containing many ova. x 75. Carried by the blood stream, ova may lodge in distant parts.



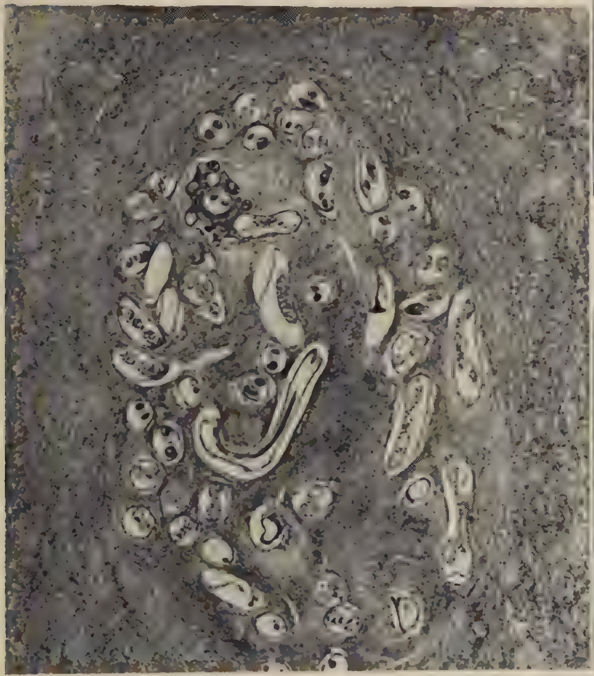
Pulmonary distomiasis, *Paragonimus westermani.* Adult trematode in cystoid space which develops around maturing parasites in lung parenchyma. Surrounding zone of inflammation and fibrosis. x30.

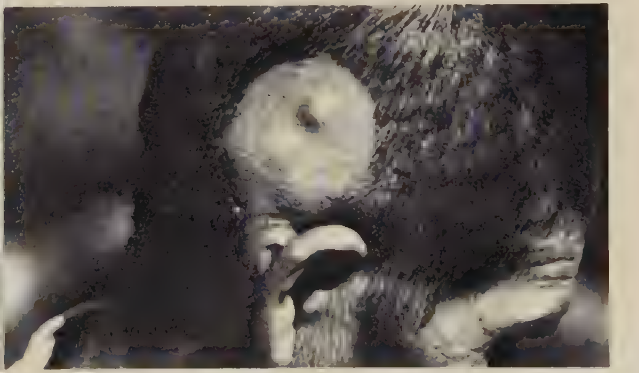


Paragonimiasis, brain. Wall showing collagenous capsule with layer of eggs and necrotic contents. x275.



Myiasis, palate. Granulomatous mass about oro-antral fistula produced by destructive burrowing and invasion of fly larvae which have developed from deposited ova.





Onchocerciasis. *Onchocerca volvulus* localizes in the subcutaneous tissue and releases numerous microfilariae only into the skin. The subcutaneous nodule is composed of adult parasites surrounded by fibrous tissue. Varied skin manifestations such as the papular thickening and focal depigmentation may be attributable to the presence of large numbers of microfilariae.

CHAPTER 13

HISTOLOGY OF THE NOSE AND PARANASAL SINUSES

Mucosa of Nose.—The nasal vestibule is lined by epidermis which contains vibrissae and sebaceous glands. It loses its stratum corneum midway within the vestibule. The tunica propria is rich in elastic fibrils and is firmly attached to the perichondrium of the septum and alae.

The mucosa is very thin but also very vascular over a triangular area on both anterior surfaces of the septum. These Kiesselbach's or Little's triangles are of practical significance because they are the frequent sites of epistaxis and of septal hemangioma. They are also subject to trauma, especially from picking the nose, and are the most frequent sites of septal perforation. There is free anastomosis over the areas between the vessels coming from the upper and lower margins. These vessels are frequently telangiectatic. The triangles are bounded posteriorly by the limen nasi, marking the junction of osseous and cartilaginous portions of the septum. The change from squamous to respiratory epithelium also occurs approximately along this line.

The mucocutaneous junction of the preturbinal region and nasal septum marks the beginning of the respiratory portion of the nasal mucous membrane. The greater part of the nasal cavity is lined by a single layer of pseudostratified columnar epithelium. This epithelium is generally ciliated, but the cilia often are lacking and the epithelium becomes stratified where it is subject to a continuous blast of air. Under normal conditions the anterior ends of the lower and middle turbinates may present areas of hyperplastic columnar epithelium or even of squamous metaplasia. These can be considered physiologic rather than actually pathologic changes. The presence or absence of cilia in these areas is dependent on the course of the inspired air. The influence of air currents on the histology of the nasal mucosa is particularly exemplified by the changes noted following laryngectomy, when the nose practically ceases to function as an air passage. Dixon and co-workers have reported these changes as increase in moisture of the anterior mucosa and replacement of squamous by respiratory epithelium.

Respiratory Epithelium.—The stratiform or pseudostratified, ciliated columnar epithelium of the respiratory portion of the nasal mucous membrane is from 35 to 75 microns thick. Cilia are normally present on all the nasal mucosal cells except those of the preturbinal and the olfactory areas. These cilia are about 7 microns long and there are 8 or 9 per cell. The ciliated cells are in the majority and quite prominent under normal conditions, but as a result of inflammation or trauma they show a ready propensity toward metaplasia to the transitional and squamous types, or they may simply lose their cilia, or they may become distended with mucus. Those of the last category are called goblet cells. As a rule, cilia reappear on subsidence of the inflammation. Basal cells presumably proliferate, mature, acquire cilia, and replace the deteriorated and desquamated columnar cells.

Nasal Glands.—Glands of the branched tuboalveolar type are abundant in all parts of the nasal cavity except the ethmoidal region and near the roof of the nose where they are less numerous. Their excretory ducts open onto the surface of the mucosa and their orifices often can be detected by the naked eye. Ciliated epithelium continues downward for a short distance into the ampulla of the gland ducts before the rather abrupt transition to nonciliated cuboidal cells begins. Mixed serous and mucous acini are encountered, a preponderance of the mucous type indicating increased activity of the glands in response to catarrhal inflammation and especially to an allergic state.

Olfactory Mucosa.—The mucous membrane of the olfactory region (upper third of the septum, the superior, and at times the middle turbinates) is unique in structure, function, and appearance. Characterized by an absence of nuclei near the surface, the epithelium consists of olfactory cells, small basal cells, and sustentacular cells. Ciliated columnar cells are normally absent and there is no visible basement membrane. The stroma contains lymphocytes and special serous glands of tubular rather than tuboracemose type, known as Bowman's glands. The olfactory cell is a fusiform bipolar neuron with a peripheral dendrite that terminates on the surface as an olfactory hair, and a central axon which joins the olfactory nerve. Unlike the other mucosal cells, but like any other nerve cell, the olfactory cells are not expendable. Trauma, polypoid degeneration, and inflammation involving the olfactory area can result in permanent loss of the sense of smell.

It is impossible in routine preparations to detect the minutiae of the histology of this highly specialized tissue, but the grosser differences are appreciable by comparing the hematoxylin and eosin stains of the two membranes included in the following plates.

Nasal Mucosa.—In stained sections the thickness of the nasal mucous membrane varies from 0.1 to 2.0 mm., being greatest over the lower part of the inferior turbinate and least over the lateral wall of the superior meatus (ethmoidal region). In most places it is between 0.25 and 1.00 mm. and varies with the development of the connective tissue, the blood vessels including the cavernous sinuses, and the glands.

The nasal mucous membranes have a rich supply of glands and blood vessels. A mass of venous channels overlies the arterial supply and a striking multiplicity of neatly arranged vessels appears when the turbinates are injected by special methods. The venous and arterial strata are connected by an elaborate system of venocapillary and arteriocapillary anastomoses supplemented by a general network of capillaries. This erectile tissue, comparable to the corpora of the penis, is well developed over the inferior turbinate, the overhanging border of the middle turbinate, and the adjacent parts of the nasal septum. The larger channels appear in the deeper strata and the smaller ones nearer the surface. The walls of these vessels are supplied with elastic tissue and muscle fibers which are developed to a degree ordinarily associated with arteries. The vasomotor mechanism of the nasal blood supply is both sensitive and complicated and the presence of the erectile tissue suggests a dual nerve control. The sensitiveness of the nasal mucosa to autonomic nervous influence is well illustrated by the studies of Holmes and co-workers, who found readily detectable changes in the nasal mucosa to "noxious stimulation inside the nose . . . and numerous threatening life situations."

Mucous Sheet.—The outer cells of the skin become keratin, while the epithelium and glands of the respiratory passages elaborate mucus. These two materials act as expendable protective coverings and serve as the first lines of defense against the invasion of infectious agents. The mucus not only acts as a mechanical protection by catching and holding dust, powders, pollens, bacteria and fungi, but it also contains an active bacteriostatic substance, lysozyme. This is present also in tears and sputum, but seems to be most potent in tears.

The mucous sheet is moving constantly backward and downward toward the pharynx under the influence of the cilia of the respiratory epithelium. The anterior third of the nasal mucosa, where the inspired air first strikes, shows relatively little ciliary activity and the movement of the mucous layer is slow in this region; it may require fifteen minutes or half an hour for it to move a few millimeters. If for any reason the currents of air are deflected, the exact distribution of this relative inactivity is altered. The greatest ciliary activity appears to be in the meatuses. Moving at the rate of 4 to 6 mm. a minute, it travels from the anterior attachment of the middle turbinates to the opening of the pharynx in from four to ten minutes. The drainage from the septum is downward and backward to the posterior margin of the soft palate. Mucus on the floor of the nasal cavity moves directly backward to the upper surface of the soft palate.

The mucous membranes of the respiratory passages are, in effect, external body surfaces, and are as well adapted to a protective role as is the skin. Semenov insists that the mucous blanket deserves greater respect and consideration than it usually receives. Hilding has emphasized the vital importance of the ciliated respiratory epithelium because of its function of conditioning air for the lungs and that of its cilia in relation to the mucous blanket. In its ciliary activity its vigorous attempts to move excess mucus from bronchi and sinuses may be deleterious, in the former producing atelectasis, and in the latter, vacuum headaches.

The changes in the nasal mucosa with increasing age have been studied by Hollender. He found no significant changes in the epithelium; absence of diffuse lymphatic tissue but some increase in fibrous connective tissue in the subepithelial stroma; no significant change in the mucosal glands or corpus cavernosa; and more prominent osteogenesis than osteoclasis in the bony structures.

PARANASAL SINUSES

The relationships between the paranasal sinuses and the nasal cavities and the character of the bony framework are shown in the illustrations. The importance of the relationship of the maxillary sinuses with the alveolar process and with the mouth is emphasized in the section on rhinosinusitis.

Mucosa.—The normal sinus mucosa is very thin, but varies in thickness in the several sinuses. The surface is perfectly smooth and is covered by a single layer of pseudostratified, ciliated columnar epithelium.

The principal function of the sinus mucous membrane in early life is that of pneumatization of bone. This function begins in the embryonic paranasal cavities and continues for several years after birth. The mucous membrane of the paleosinus (embryonic stage) is thick, richly endowed with glands, and the periosteal aspect or planum resortiones is roughened. As pneumatization proceeds the membrane becomes thinner and the glands tend to disappear except near the ostia of the sinuses.

In postoperative repair the old mucosa may be replaced by firm scar tissue covered with epithelium which may have lost its respiratory character. New bone is deposited on the surrounding walls by the periosteal portion of the mucosa.

Sinus Glands.—There are relatively few mucous glands in the sinuses and their distribution is limited to the region of the ostia except in the presence of prolonged infection. Large areas of sinus mucosa are totally devoid of glands. The acini of the individual glands are not as closely packed as are those in the nasal mucosa. The normal location of the glands is between the loose and compact layers of stroma. The glands are predominantly serous. The round nuclei of the serous cells are located near the base of the cell; those of the mucous cells are oval and compressed against the basement membrane.

In the maxillary sinus there are small compound tubo-alveolar glands, but farther from the ostium the glands are simple and become thinner, more scattered, and eventually disappear. The lateral walls of the maxillary sinus in their normal state are devoid of glands. In the ethmoidal sinuses a few branched tubular glands are seen; but in the frontal and sphenoidal sinuses glands are rare and simple.

Blood Supply.—In the living state, the sinus mucosa is a pale yellowish ivory. The nasal mucosa by contrast has a faintly pinkish blush from its rich vascularity, a quality which in part explains the difference in the rate of healing of the two mucosae. The nasal mucosa recovers from the same insult much more rapidly than does the sinus mucosa. The membrane lining the paranasal cavities plays no part in the warming and moistening of inspired air. The thin and delicate mucosa requires few blood vessels to nourish it and thus is pale because it transmits the color of the bone beneath it. When a sinus is the seat of inflammation with dilatation of its blood vessels, or of chronic sinusitis with granulation tissue formation, its lining becomes reddened. Hyperplastic and polypoid membranes often exhibit less hyperemia and appear grayish or yellowish (Semenov).

The larger arteries and veins course in the deep layer of the submucosa and are continuations of vessels that penetrate the bony walls and slant gradually through the periosteal connective tissue. The capillaries can be seen just under the epithelial layer, and in hyperplastic membranes they seem to spring upward, almost at right angles.

Sinus Connective Tissue.—The membrane lining the sinuses is a mucoperiosteum consisting of two layers of connective tissue, one a loose subepithelial, the other a compact periosteal layer. Variations are common, however, and a membrane may be predominantly loose or predominantly compact, or others may have areas of both descriptions.

The important characteristic of the loose areolar layer of connective tissue is its tendency to become extremely edematous. Large lakes of fluid may accumulate in chronic inflammatory reactions and cast shadows in roentgenograms. Venous stasis with consequent increase in hydraulic pressure distends the tissue spaces, pushes the fibers apart, and thus throws the surface of the mucous membrane into polypoid folds. In cases of polypoid hyperplasia one may find, in association with the edema, young stellate and spindle-shaped connective tissue cells.

The periosteal layer consists of a dense membrane of white fibrous tissue that merges indefinably with the overlying loose tissue and is firmly bound to the bone beneath. It functions as does periosteum and is capable of osteoclastic and osteogenic activity when disturbed.

The deep layer of connective tissue seldom suffers degenerative changes, whereas the upper loose layer is actively involved in inflammatory reactions.

The mucous membrane lining the maxillary sinus differs from that of other sinuses (frontal, ethmoidal and sphenoidal). On its medial wall the tunica propria is generally thicker, well supplied with blood vessels, and contains a fair number of submucous glands. This portion of the sinus bears a faint resemblance to the respiratory membrane of the nasal fossa. It is 0.2 mm. in thickness while the lateral portion is less than 0.1 mm., is less vascular, and contains no mucous glands.

THICKNESS OF MUCOUS MEMBRANES

	Normal Variations mm.
Maxillary sinus:	
Medial wall	0.3 –1.0
Lateral wall	0.1 –0.5
Frontal sinus	0.07–0.3
Ethmoidal sinus	0.08–0.4
Sphenoidal sinus	0.07–0.5

The **bony framework** of the nose is so designed that a maximum of mucosal surface is exposed to the inspired air. This is accomplished by the turbinate bones. The structure of the bone forming most of the framework of the sinuses as well as that of the nose differs from ordinary cancellous bone in that the spaces between the trabeculae, instead of being filled with fatty marrow, are largely occupied by connective tissue richly supplied with blood vessels and lymphatics. These vessels communicate freely with the overlying mucosa and can therefore assume a very important role in disseminating inflammations. Because of this relationship and the frequency of sinus infections, osteitis and thrombophlebitis occur more readily in these bones than in bones generally.

Another structural difference is the character of the periosteum. This is not a distinct, sharply defined membrane as is the periosteum generally, but it fuses imperceptibly with the stroma of the mucosa. Its periosteal character, however, becomes evident when it is irritated, because it then asserts its osteogenic capacity.

Mention must be made here of the **lacrimal ducts** and **sacs** that are often considered to be entirely in the province of the ophthalmologist. As will be noted, however, in the following illustration of a frontal section of a fetal head, anatomically they certainly are within the province of the otolaryngologist as well. Furthermore the cause of dacryocystitis is commonly within the nose—chronic rhinitis, nasal polyp, deflected septum, etc. It will be remembered that the sac lies in the lateral bony wall of the nose, just anterior to the middle turbinate, and that its orifice is under the anterior end of the inferior turbinate.

Clinically, DACRYOCYSTITIS manifests itself in the eye by swelling of the nasal ampulla and by the appearance of exudate on pressure over the inner canthus. The primary symptom of interference with lacrimal drainage is tearing.

Suppurative inflammations may break through the sac and give rise to cellulitis about the inner canthus of the eye, or to a fistula when the infection points and ruptures onto the surface; a cyst may develop when the contents do not escape. Intranasal drainage or excision of the sac may be necessary.

Interference with lacrimal drainage by tumors of the nose, and especially of the maxillary sinus, is discussed later.

Primary tumors of the lacrimal mucosal epithelium are rare, but a carcinoma developing in the sac is illustrated in the following plates.

CYSTIC TURBINATE (CONCHA BULLOSA)

There is one clinical entity involving the nose which is on a developmental basis and is so frequent as to be appropriately included here. It is concha bullosa or pneumatization of the middle turbinate.

The ethmoidal air cells tend to expand in all directions until they reach compact bone, a suture line, or cartilage. They may, therefore, invade the nasal septum, the supreme and superior turbinates and—of clinical significance—into the pendulous portion of the middle turbinates. Incidentally, Van Alyea reports supreme turbinates in 67 of 100 specimens examined and in 38 of these, ethmoidal cells were present, all draining into the supreme meatus.

The presence of air cells in the middle turbinate has been recognized since 1739. It is not a particularly rare condition. It is usually unilateral and is more common in women. There have been several explanations for the lesion, including the dubious possibility of an infolding of surface mucosa as a result of an inflammatory or mechanical factor, but it is now generally accepted that it is a developmental entity resulting from the inclusion in the middle turbinate of mucosa of the ethmoidal sinus. As a consequence there is an isolated air cell or several cells lined by respiratory epithelium, or an air cell connected with the ethmoidal labyrinth by a persistent communication. Such a communicating structure is liable to the same inflammatory reactions as is the parent sinus.

The pneumatization may be sufficiently extensive to result in anomalous size of the turbinate, which is of clinical significance and requires attention, or the accumulation of mucus or exudate can cause expansion and softening of the walls to the point of obstructing the nostril.

The aberrant cells usually contain air, but they may contain fluid because of mucoid activity of the epithelium, purulent material as a result of infection, or the mucosa may show areas of polypoid hyperplasia. These conditions are all secondary to the basic developmental defect (Baum). Infection in the cell occasionally erodes through the surface and produces a fistulous opening in the nasal cavity.

The epithelium exhibits the same tendency to squamous metaplasia in response to inflammation as does that of the normal respiratory cavities. Mucosal glands may be entirely absent, or they may be present and even hypertrophied. The lining membrane has not the vascularity of the turbinal mucosa. The bony wall varies in thickness indirectly with the size of the cell, and it can be reduced to a single lamella of bone or occasionaly even be absent. In this case a sac-like structure is attached by a pedicle, usually to the posterior end of the turbinate.

PERFORATION, NASAL SEPTUM

Perforation of the nasal septum is another clinical entity so dependent on the anatomy and histology of the part as to warrant its inclusion at this point. Aside from the details of vascularity, character of mucosa, and vulnerability to trauma, there is the tenuous nature of the septal cartilage, particularly in its center. A coronal section will demonstrate the very thin center and the flare to thicker borders.

Formerly the commonest causes of septal perforations were syphilis and operative trauma. These two causes have been largely eliminated and now tumors and infections secondary to trauma are the commonest. Occasionally perforation results from one of the granulomatous infections, especially those due to fungus. A specimen recently received is an example of perforation in a 52-year-old man who had had rheumatic symptoms for some time. Biopsy had previously shown a lesion on his elbow to be a rheumatic nodule. Nose bleeds are a common symptom of rheumatic fever. The case suggests the possibility that the nasal septum may be involved in systemic "collagen" disease.

The influence of thromboangiitis on the extension of a necrotizing process is discussed in the chapter on gangrene. Several instances of perforation due to nonspecific infections and to carcinoma are included in the following illustrations.

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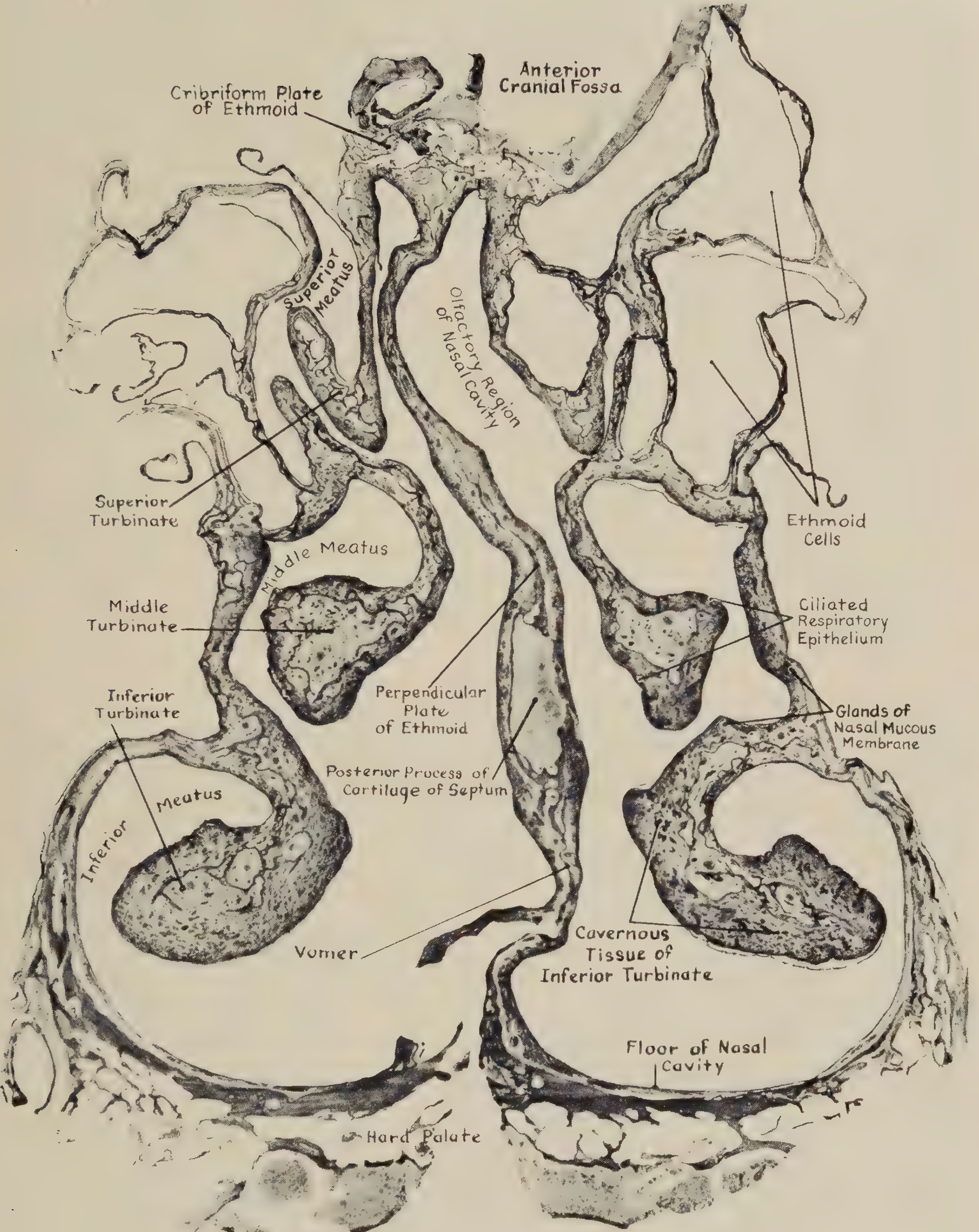
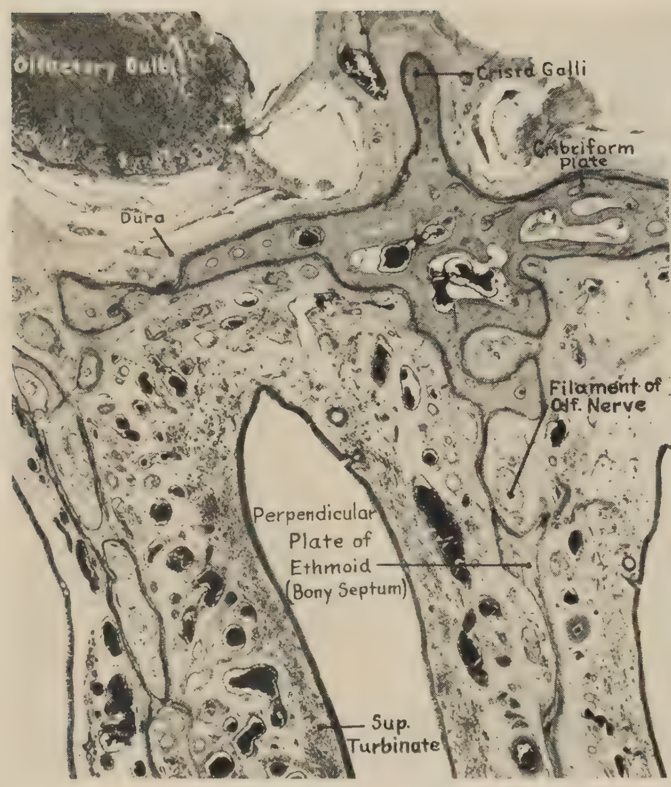
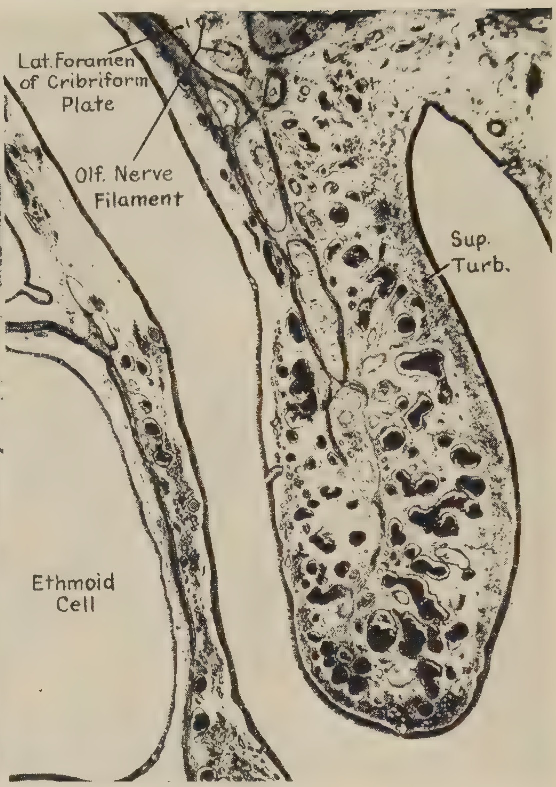

Anterior Cranial Fossa
Cribriform Plate of Ethmoid
Superior Meatus
Olfactory Region of Nasal Cavity
Superior Turbinate
Ethmoid Cells
Middle Meatus
Middle Turbinate
Ciliated Respiratory Epithelium
Inferior Turbinate
Perpendicular Plate of Ethmoid
Glands of Nasal Mucous Membrane
Posterior Process of Cartilage of Septum
Inferior Meatus
Vomer
Cavernous Tissue of Inferior Turbinate
Floor of Nasal Cavity
Hard Palate

Coronal section at level of posterior part of nasal cavity to include superior, middle and inferior turbinates. Fracture of the floor on the left during preparation of the section has caused deviation of the septum and deformity of the ethmoidal cells on that side. Note the very thin septa between the ethmoidal cells and between them and the superior meatus. (H. Semenov)

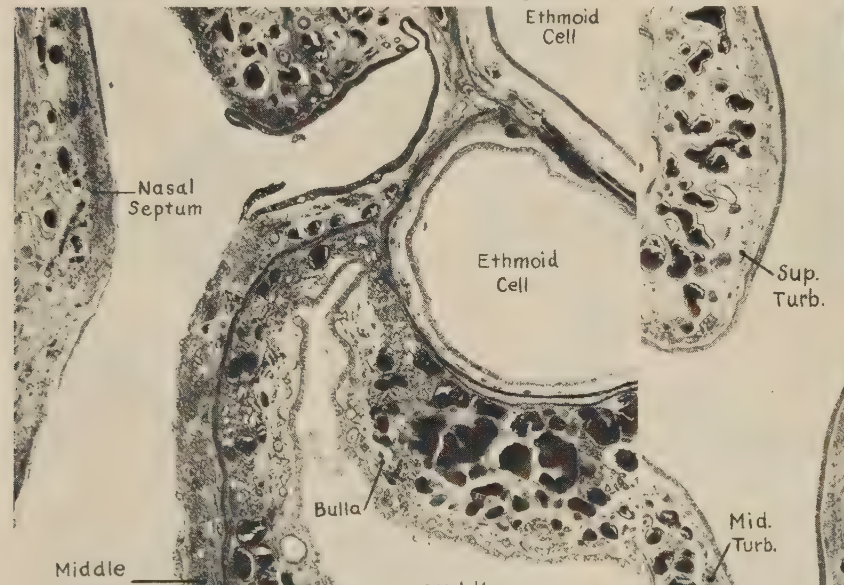
HISTOLOGY


Olfactory Bulb
Crista Galli
Cribriform Plate
Dura
Filament of Olf. Nerve
Perpendicular Plate of Ethmoid (Bony Septum)
Sup. Turbinate

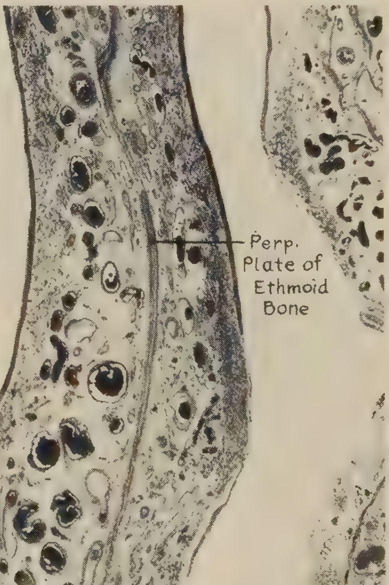
Olfactory region of nasal cavity. Parts of the ethmoid bone included are: the cribriform plate with crista galli, the perpendicular plate (nasal septum), and the superior nasal concha. Note filaments of olfactory nerves in foramina of cribriform plate. x 18.


Lat. Foramen of Cribriform Plate
Olf. Nerve Filament
Sup. Turb.
Ethmoid Cell

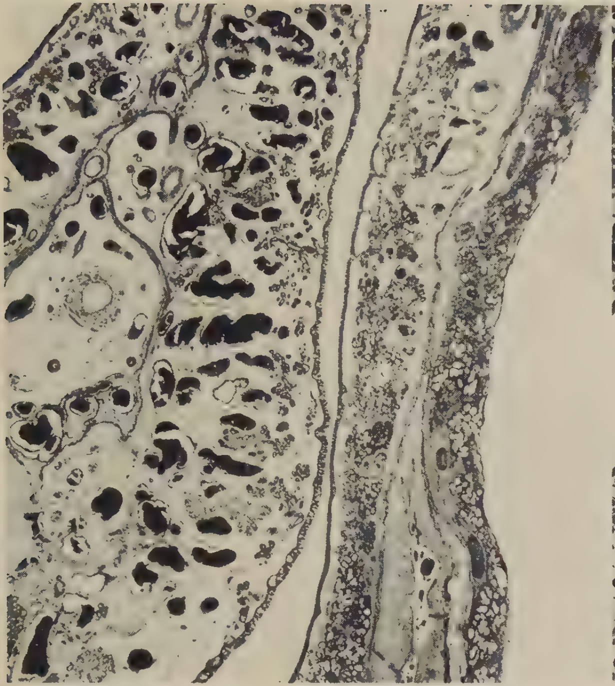
Superior meatus in posterior superior part of lateral wall of nasal cavity. Superior turbinate at right; lateral nasal wall and parts of two ethmoid cells at left. x 13.


Ethmoid Cell
Nasal Septum
Ethmoid Cell
Sup. Turb.
Bulla
Mid. Turb.
Middle Turbinate
Middle Meatus

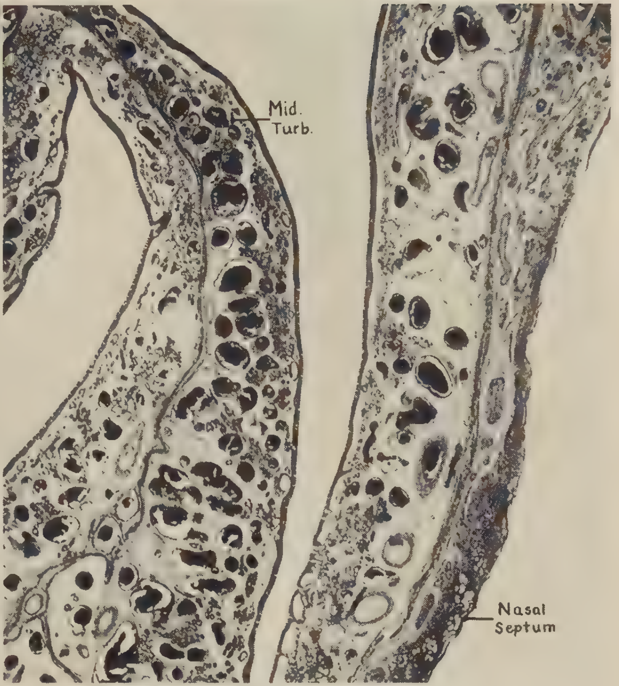
Middle meatus between middle turbinate and ethmoid bulla. The bulla is prominent because it contains a large ethmoid cell which also impinges on attached portion of turbinate. x 15.


Perp. Plate of Ethmoid Bone
Mucosa of Nasal Septum

Nasal septum, slightly deflected from median plane as is usual. Level of section is just inferior to that in upper left figure. x 15.

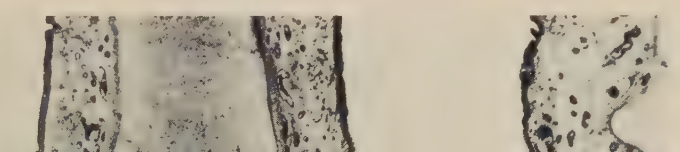


Bony septum and middle turbinate (pendulous part) just posterior to insertion of cartilaginous septum. Narrowed meatus with only moderate deviation of the septum. x 14.

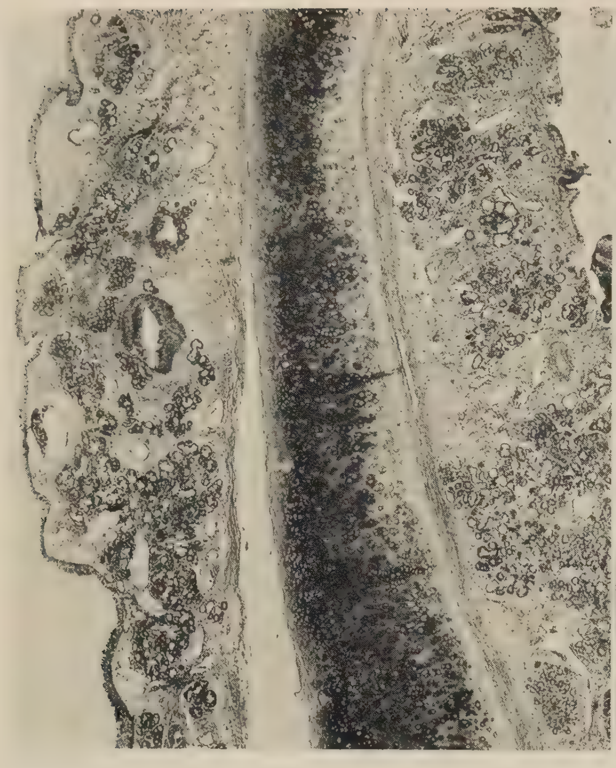


Septum and middle turbinate (attached part). Mucosa is thicker and contains more numerous cavernous vessels and glands on medial convex surface of turbinate than on lateral surface. Seromucinous glands more numerous in lower than upper part of septum. x 14.

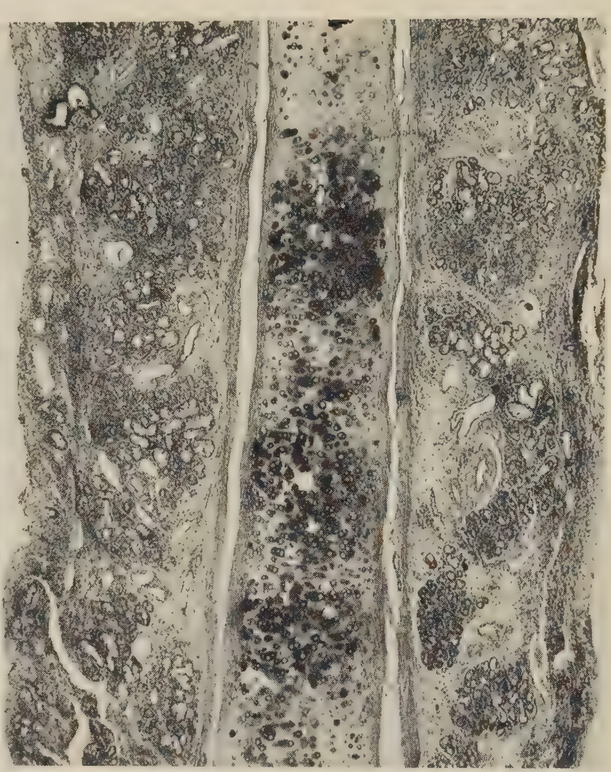
Nasal septum of 4 month fetus. Pale immature cartilage. Tubular dark foci in mucosa are epithelial downgrowths—the early developing glands. Well defined ciliated columnar epithelium. x 39.



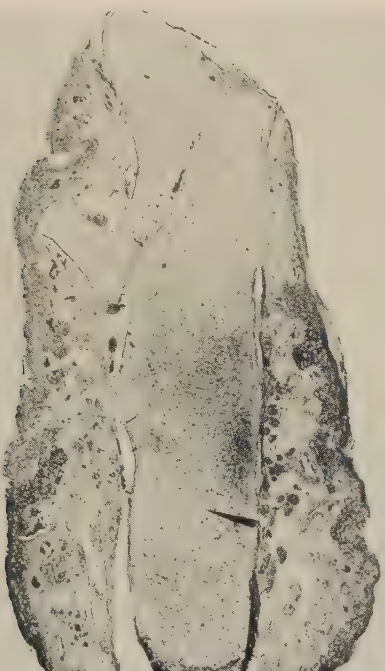
Nasal septum of 7 month fetus. More mature cartilage with prominent perichondrium. Developing glands at top, some well developed at bottom. More prominent vessels. Well differentiated respiratory epithelium with goblet cells. x 18.



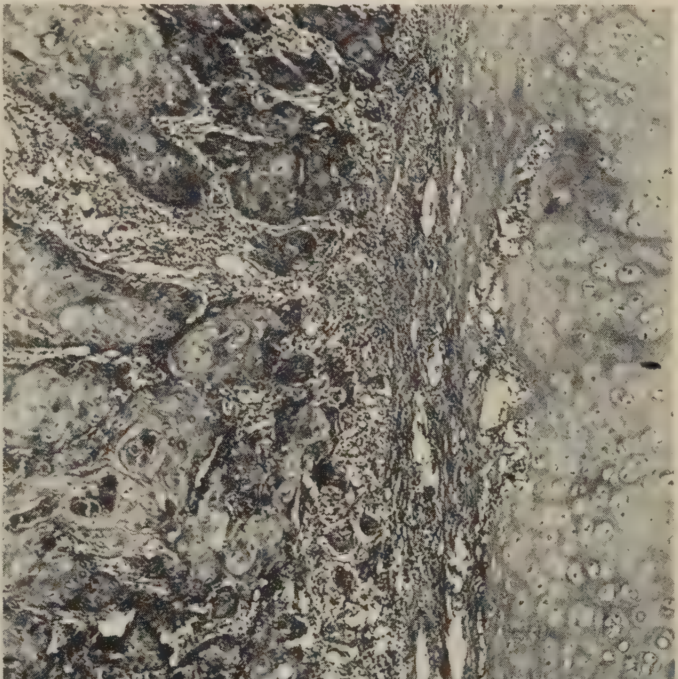
Septal cartilage takes a deep basic stain uniformly distributed. Perichondral layer is well defined; split on left is artefact. The mucosa is slightly thicker than normal. x 21.



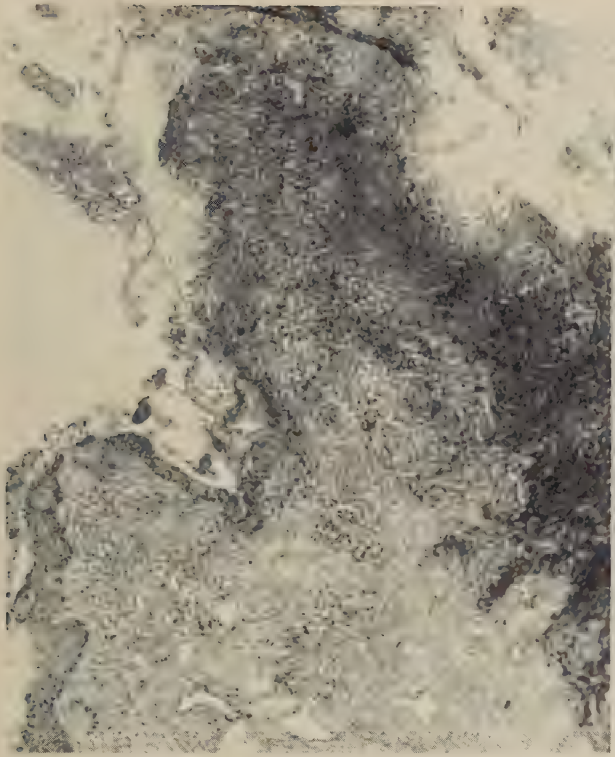
Section from septum adjacent to a perforation. Cartilage is stained irregularly; the little vacuoles represent mucoid degeneration. Perichondrium is split along normal cleavage planes. x 27.



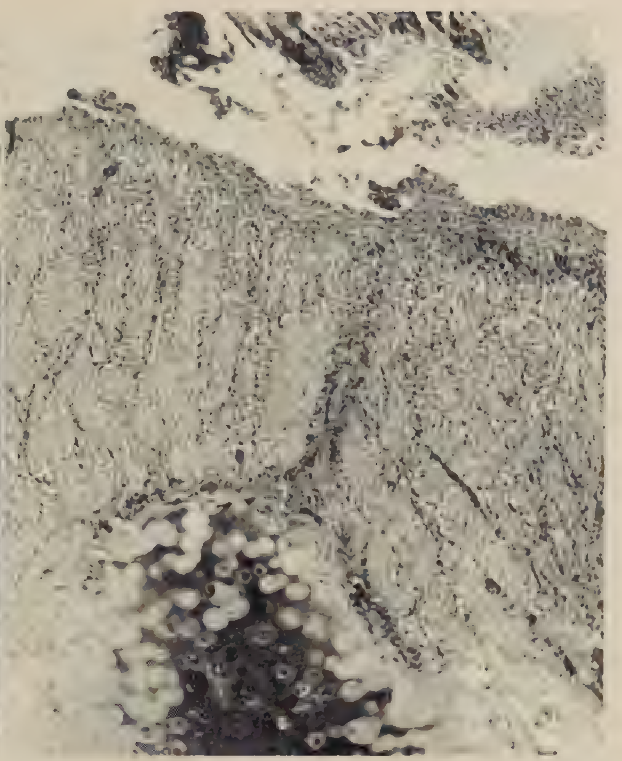
Horizontal section through septum at level of tubercle (above). At bottom, point of insertion of cartilage in bony septum. (W. Mueller, Boston).



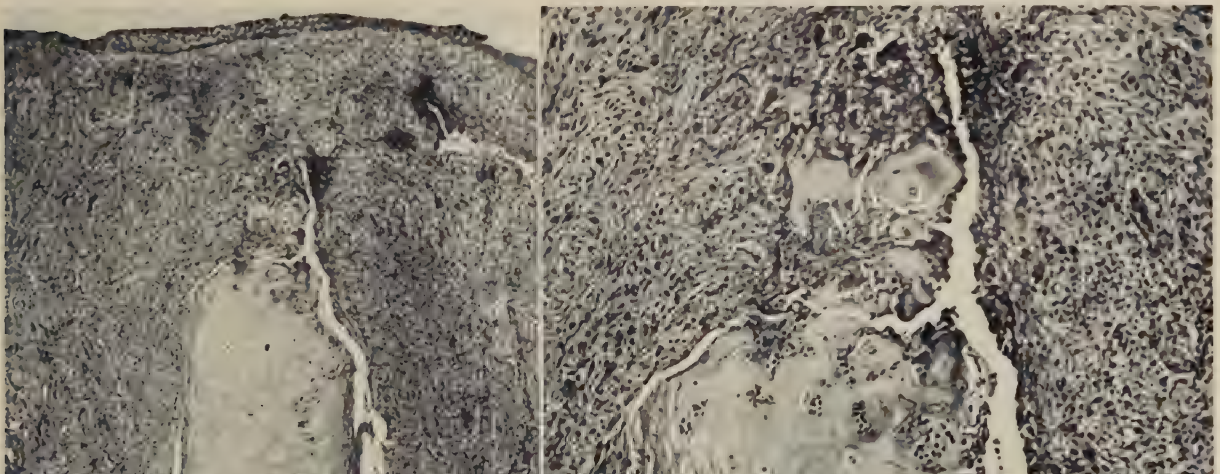
Anterior cartilaginous septum, showing marked perichondritis. A well differentiated squamous cell carcinoma has invaded to the perichondrium. x 100.



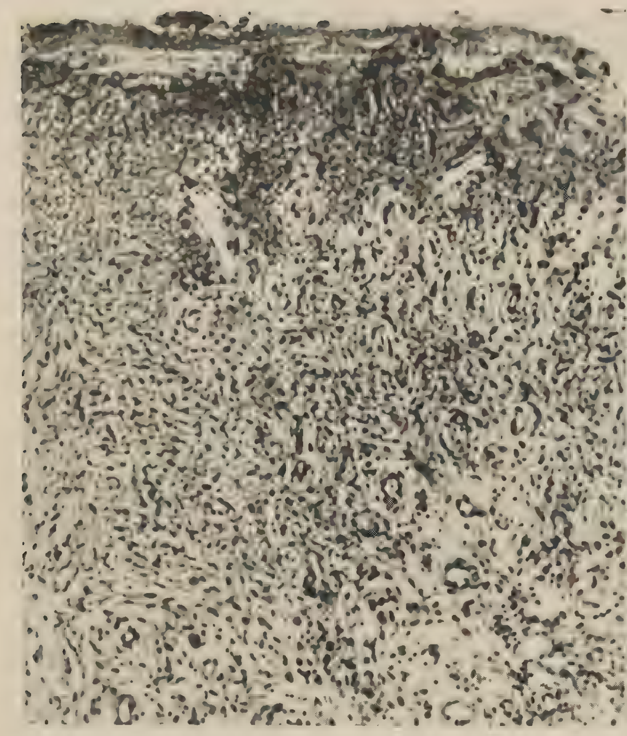
Acute ulceration in a 21 year old man with pain and bleeding for 6 months; negative Kahn test. The edge of the perforation is lined by purulent necrotic tissue. Etiology not determined. x 55.



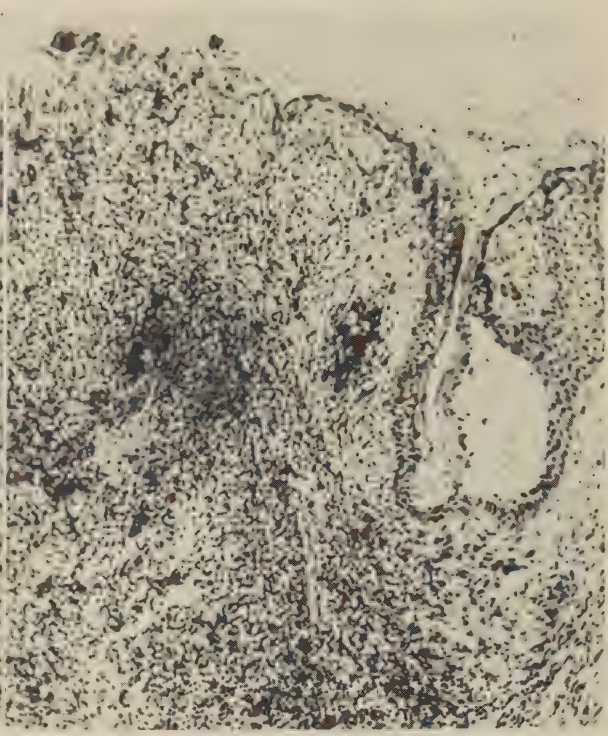
More chronic suppurative reaction in a 55 year old man with a perforation, 1 x 2 cm., of 1 year's duration. No history of trauma, surgery, or syphilis. Eroded edge of cartilage covered by granulation tissue. x 48.



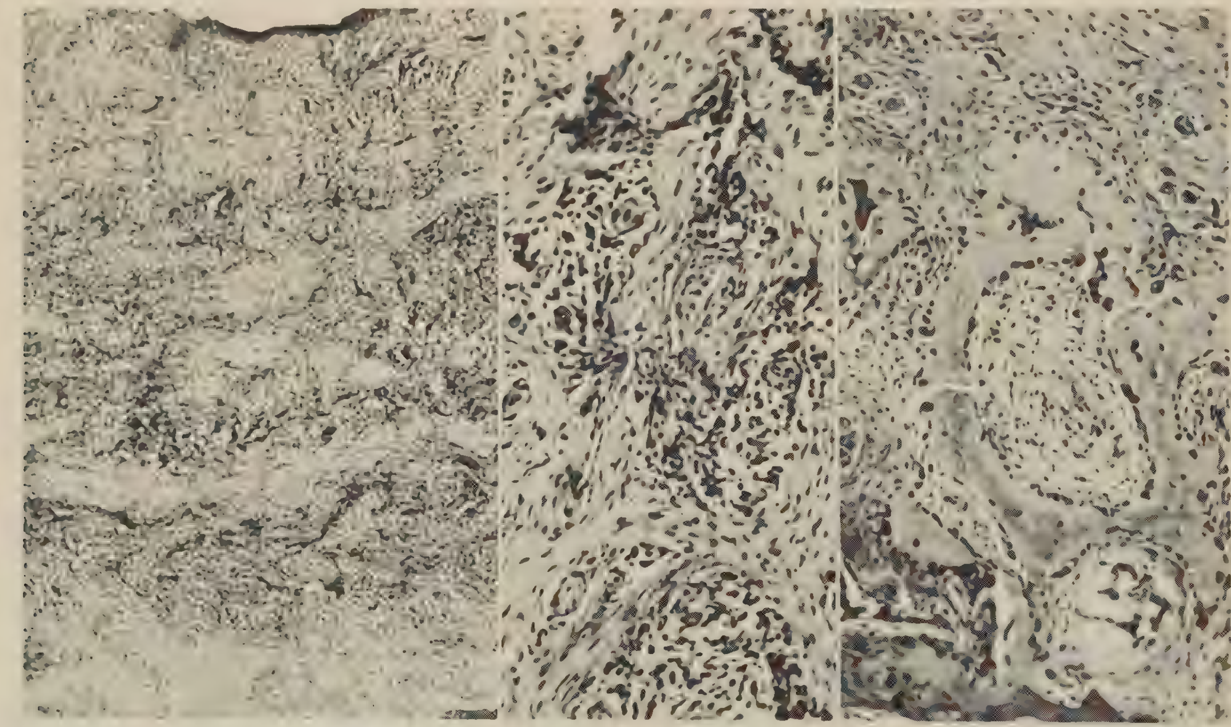
Degeneration and destruction of cartilage, active. Large perforation in man under treatment for tuberculosis. No evidence of syphilis. Left, eroded edge of cartilage covered by chronic granulation tissue heavily infiltrated by polymorphonuclear leukocytes. x 48. Right, active erosion of cartilage, with invasion by leukocytes and fragmentation of cartilage. x 105.



"Chronic" granulation tissue with surface crust of blood and necrotic debris. History of "crusting" on septum for 9 years, with perforation for 1 year. x 125.

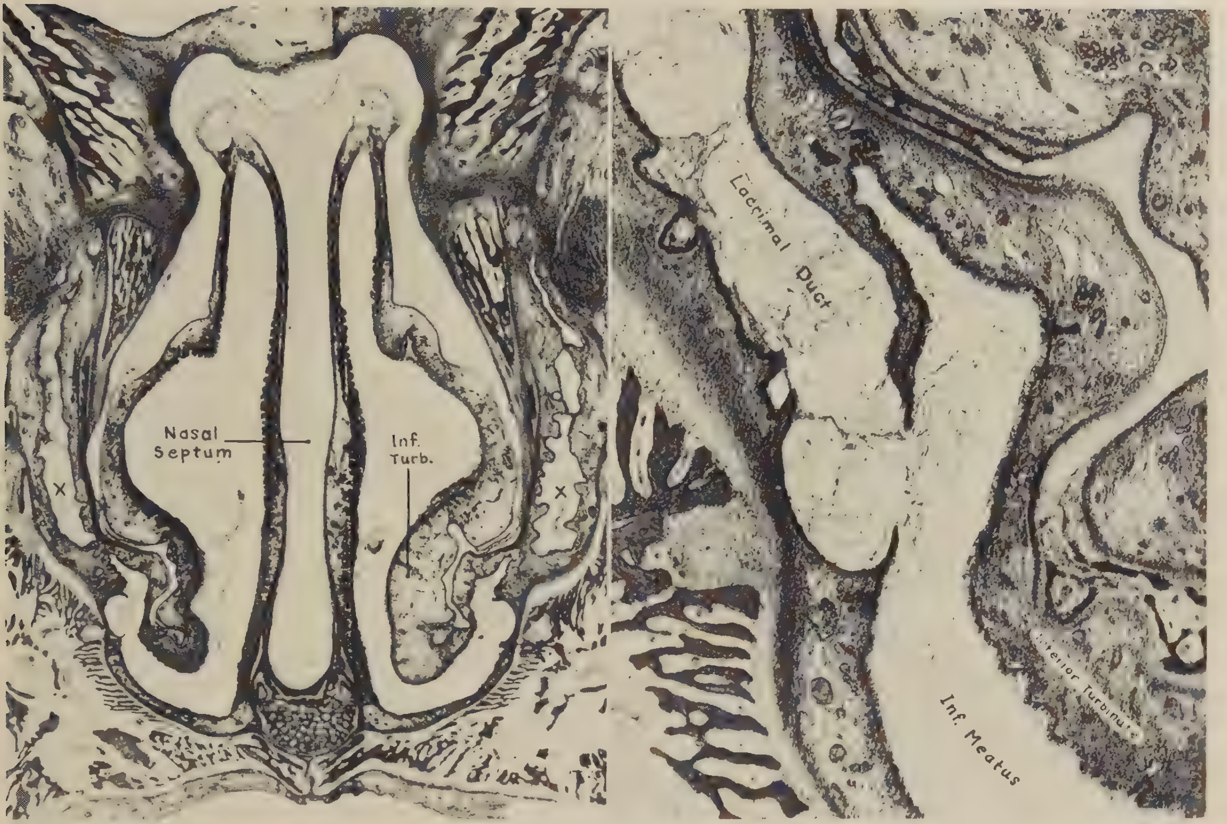


Granulomatous mass about tubercle of septum for 1 year, in a 55 year old woman with no serologic evidence of syphilis. Chronic granulomatous inflammation at edge of perforation with squamous metaplasia of adjacent epithelium. x 125.

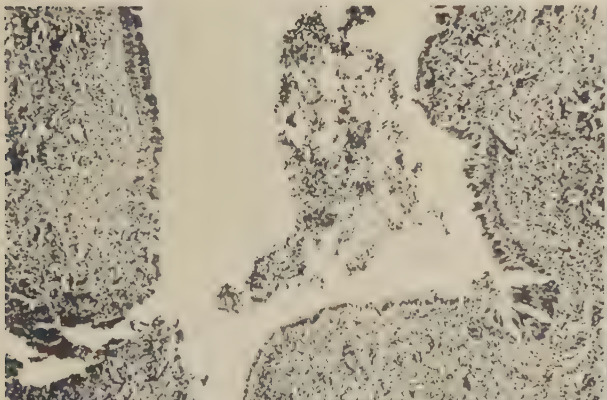


Perforation due to syphilis? Margin of perforation in a 29 year old woman with a history suggesting syphilis is dense, scar-like tissue, without purulent element. x 48. Thick-walled arteries and plasma-cell exudate suggest syphilitic infection. x 125. Perichondritis has stimulated osteoid bone formation. x 125.

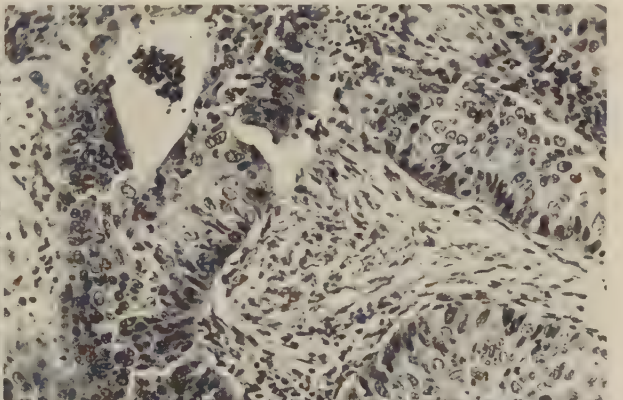
DACRYOSOLENITIS–CARCINOMA



Nasolacrimal ducts (x) in coronal sections of head of 4 month fetus, at level of anterior parts of inferior turbinate. x 8. These end in expanded orifices, provided with an imperfect mucous membrane valve, the plica lacrimalis, in the anterio-superior portion of the inferior meatus. x 37. (J. V. Cassady, South Bend, Ind.)

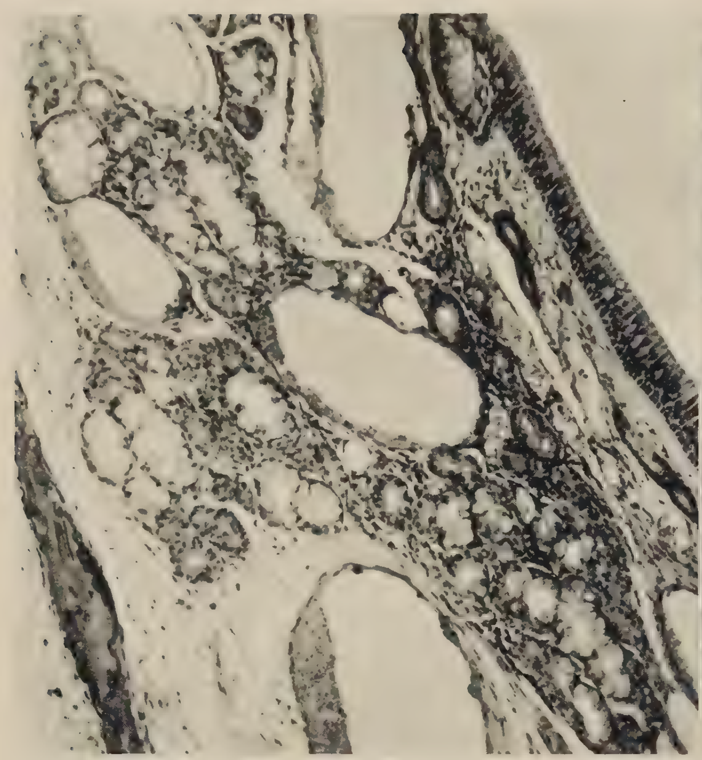


Dacryosolenitis (inflammation of lacrimal duct) accompanying dacryocystitis. Polypoid thickening of chronically inflamed mucosa. Cellular exudate in lumen and infiltrating the irregular, partially desquamated epithelium. x 60.

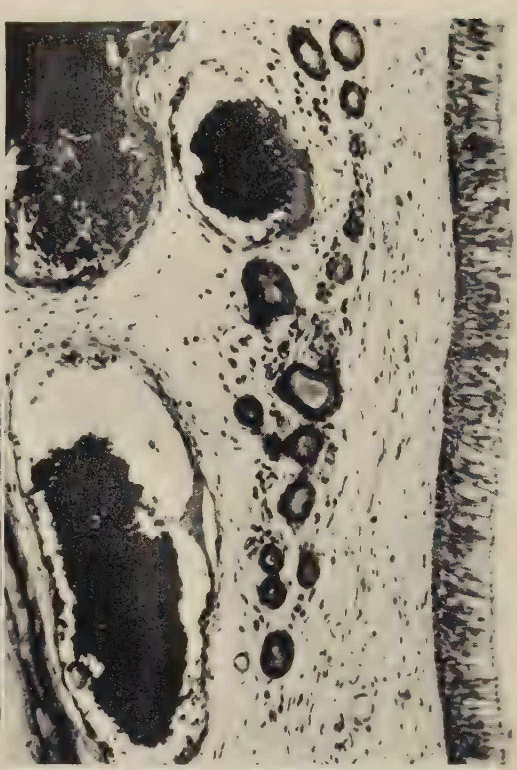


Carcinoma of nasolacrimal duct, possible case. Strands of carcinoma with suggestive epidermoid differentiation. x 160. Primary carcinoma of the duct is rare.

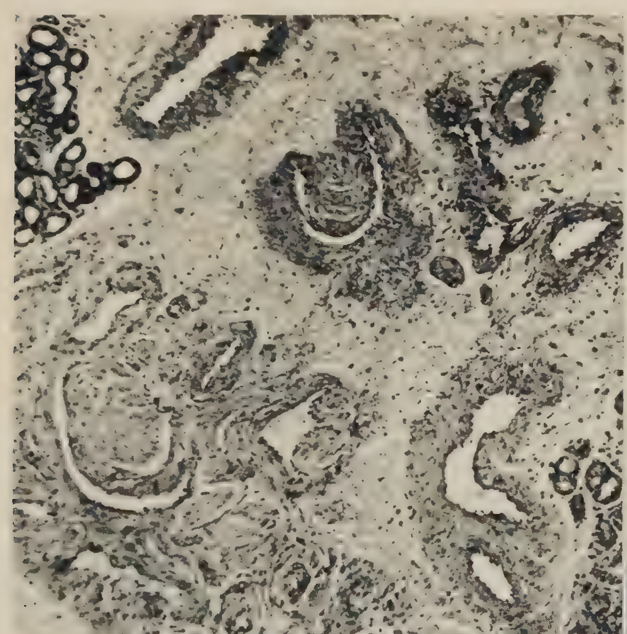
HISTOLOGY



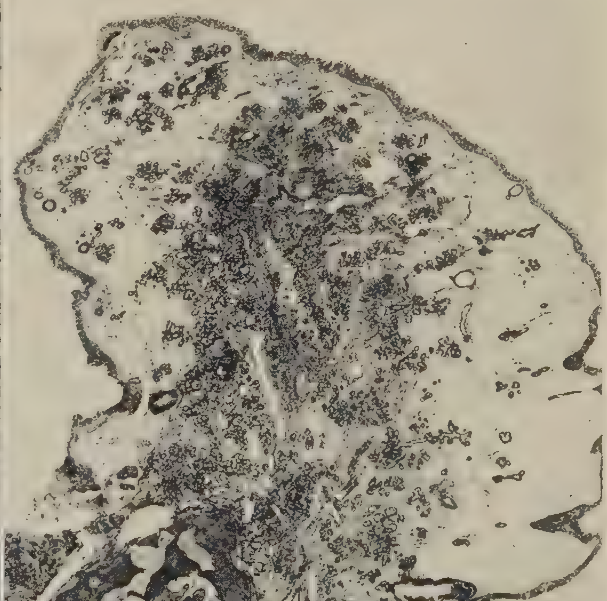
Normal turbinal mucosa varies in thickness. Ciliated respiratory epithelium; distinct basement membrane; seromucinous glands; dilated superficial veins; fibroelastic connective tissue tunica propria. x 100. (Semenov)



Thin turbinal mucosa with relatively few glands, from lateral portion of superior turbinate. x 150.

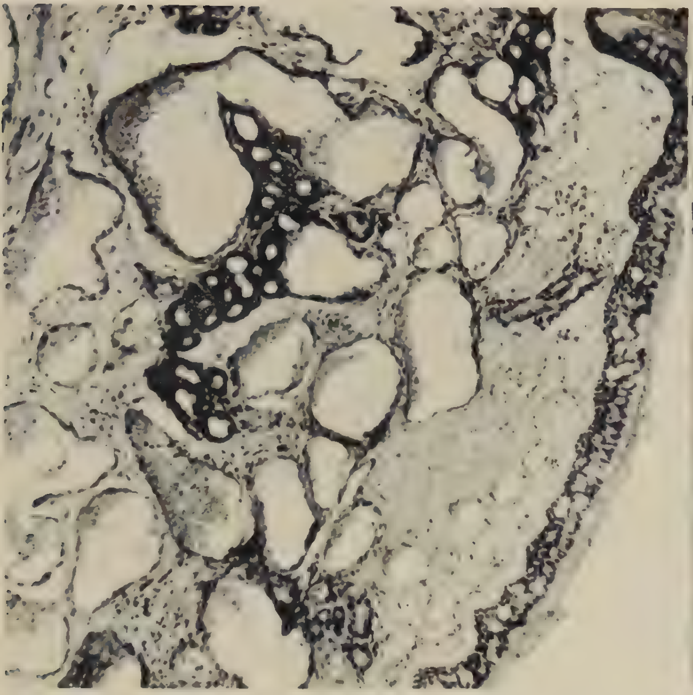


Veins of cavernous plexus of turbinate, collapsed. Abundant elastic tissue, relatively little smooth muscle. x 85. "Absence of septa containing smooth muscle differentiates this from true erectile tissue"—Maximov.

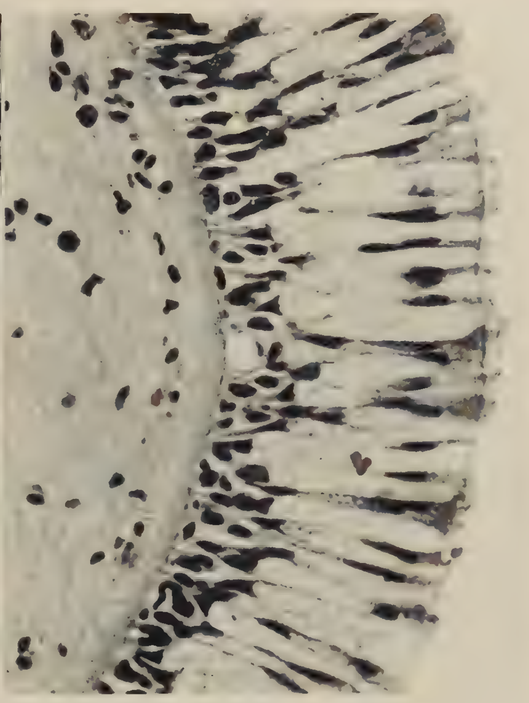


An accessory or supreme turbinate. Firm polypoid mass in roof of nose, thought clinically to be an osteoma. x 15.

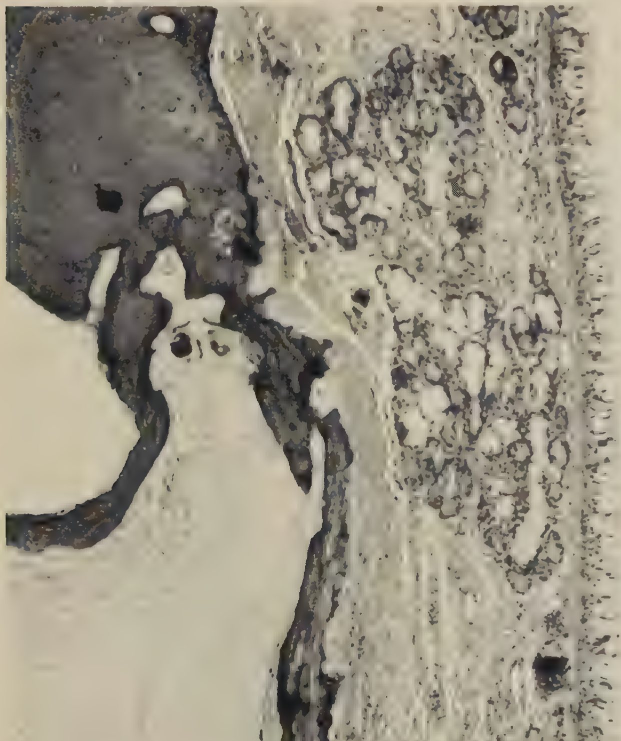
HISTOLOGY



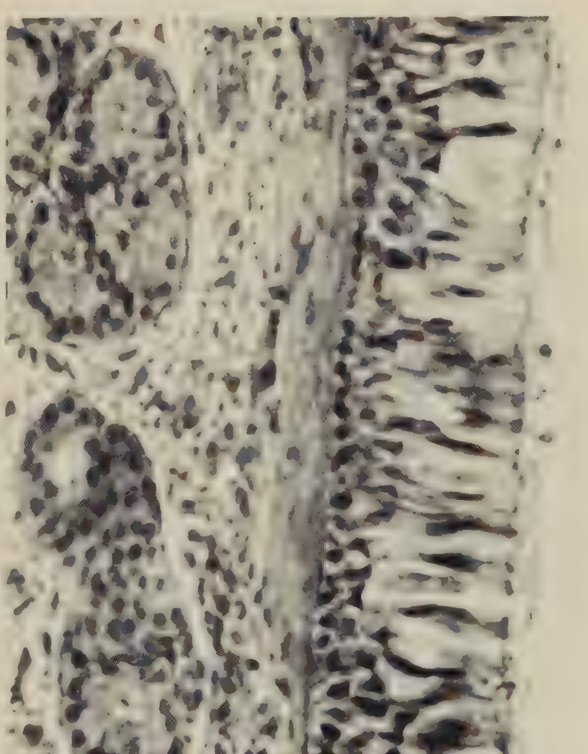
Normal turbinal mucosa with prominent cavernous vessels (inferior turbinate and parts of middle turbinate and septum). Ciliated respiratory epithelium with goblet cells and thin "mucus blanket." x 125.



Turbinal epithelium may vary with location and disease. Almost diffuse mucinous content in very tall columnar cells of part of inferior turbinate, with intervening ciliated cells (above). x 400.



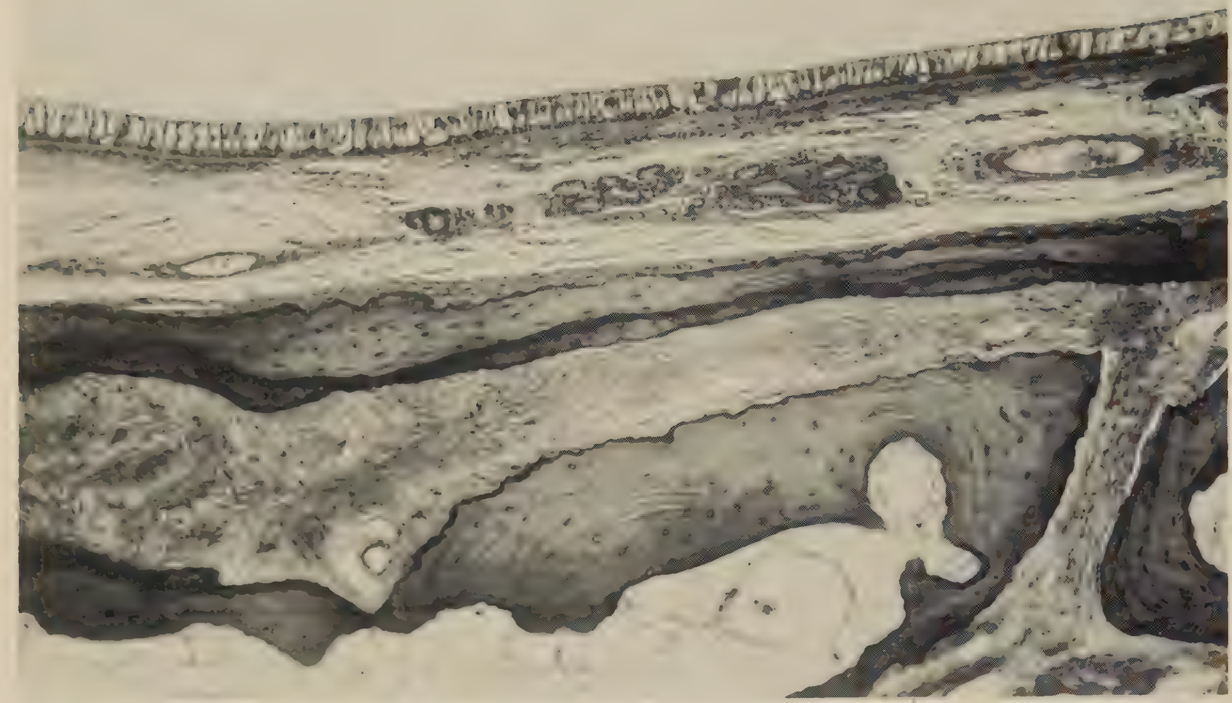
Normal septal mucosa at junction of perpendicular plate of ethmoid and cartilaginous septum. Clear foamy cytoplasm of cells of the active mucous glands well contrasted with uniform, darker, cuboidal cells of the serous glands. x 100.



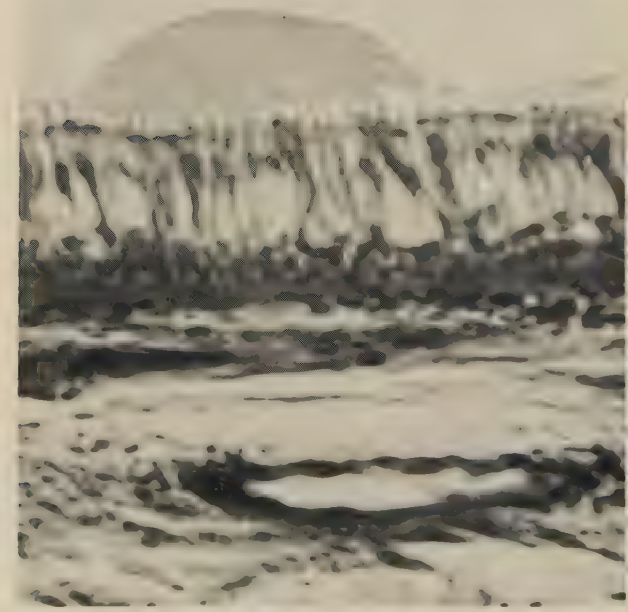
Septal epithelium. Numerous "goblet" cells in ciliated respiratory epithelium; distinct basement membrane; serous-type glands in tunica propria. x 500.

MUCOSA OF NASAL CAVITY

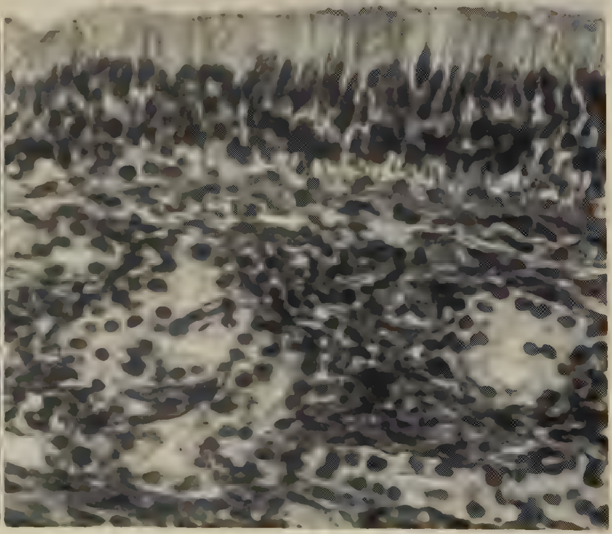
RESPIRATORY AND OLFACTORY EPITHELIUM



Floor of nasal cavity lined by relatively thin mucous membrane, lacking the prominent vascular and glandular structure of other areas. Bony floor composed of trabeculae of bone, enclosing cellular fibrous tissue above and looser fibrofatty tissue at bottom. x 100.

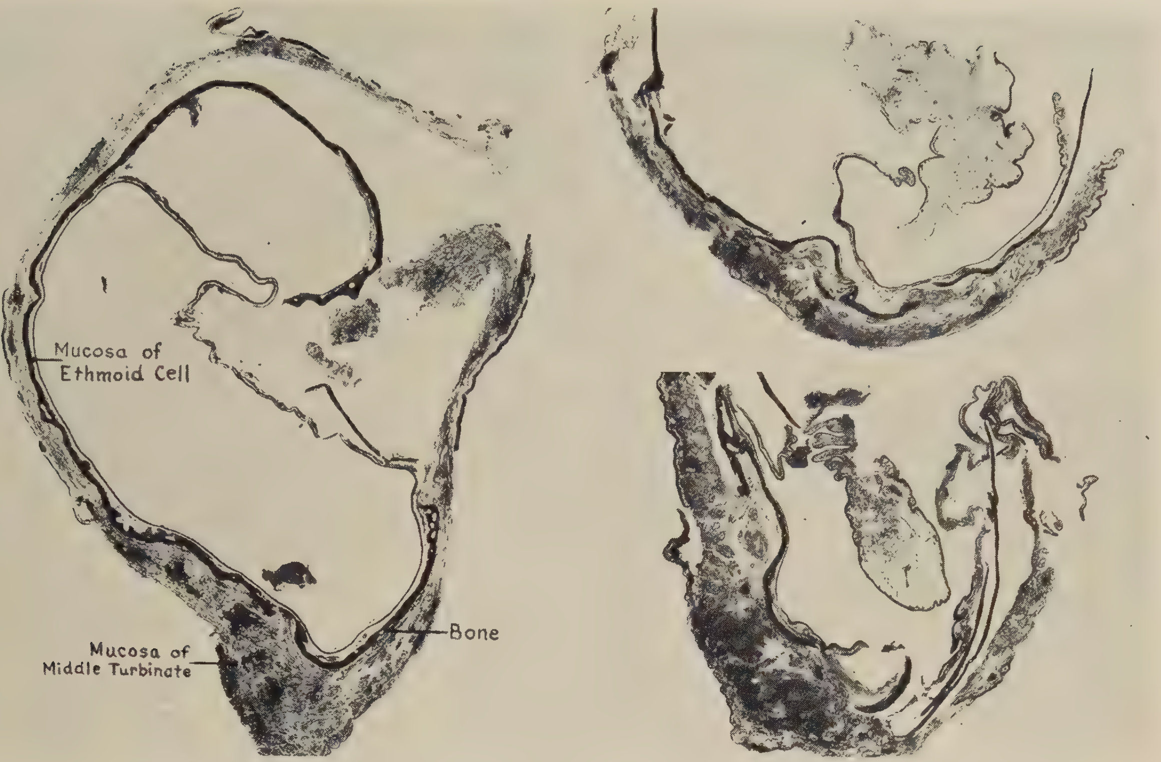


Respiratory epithelium (inferior meatus). Pseudostratified columnar ciliated epithelium. The mucosal glands and the goblet cells of the epithelium secrete the thin protective coat or mucous blanket (at top). Clearly defined basement membrane. x 500.

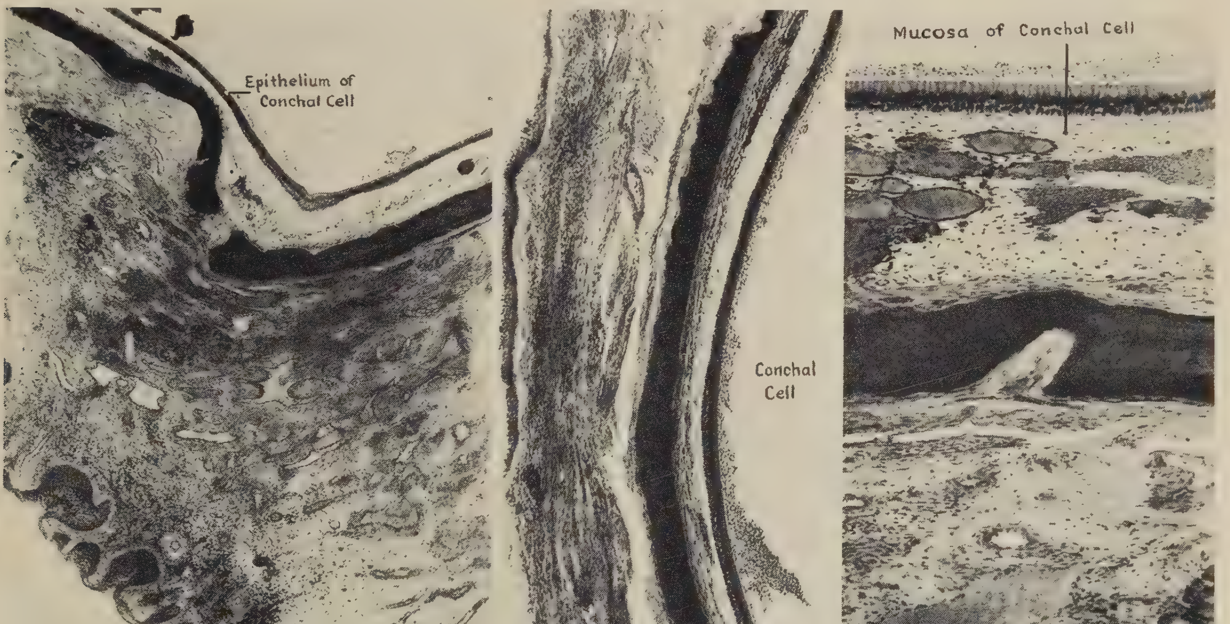


Olfactory epithelium. Upper third is devoid of nuclei. Beneath it are three irregular nuclear zones: (1) uppermost, of tall slender **sustentacular or supporting cells** with oval nuclei and pigment granules; (2) midzone, of **bipolar olfactory cells** with round clear nuclei and short, fine "olfactory hairs" at surface; (3) bottom, single layer of small **conical basal cells** with dark nuclei. No basement membrane. Bowman's glands in lamina propria. x 500.

CONCHAL CELLS
("CELLULAR TURBINATE"; CONCHA BULLOSA)

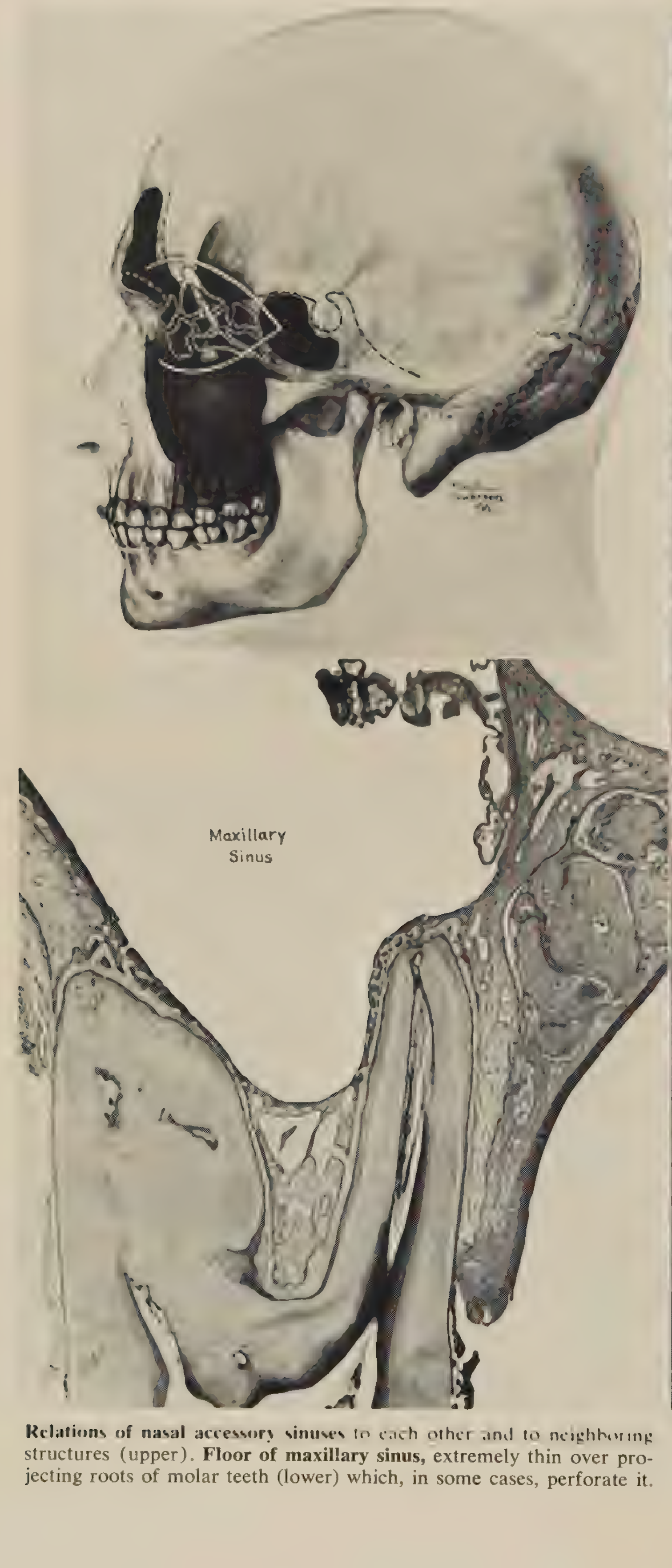

Mucosa of
Ethmoid Cell
Bone
Mucosa of
Middle Turbinate

Conchal cells. A. Ethmoid cells tend to expand in all directions and to pneumatize the upper turbinates, and the pendulous portion of the middle turbinate. x8. **B.** and **C.** Mucosa of cells may become polypoid. x8. (S. S. Hall, Clarksburg, W. Va.)

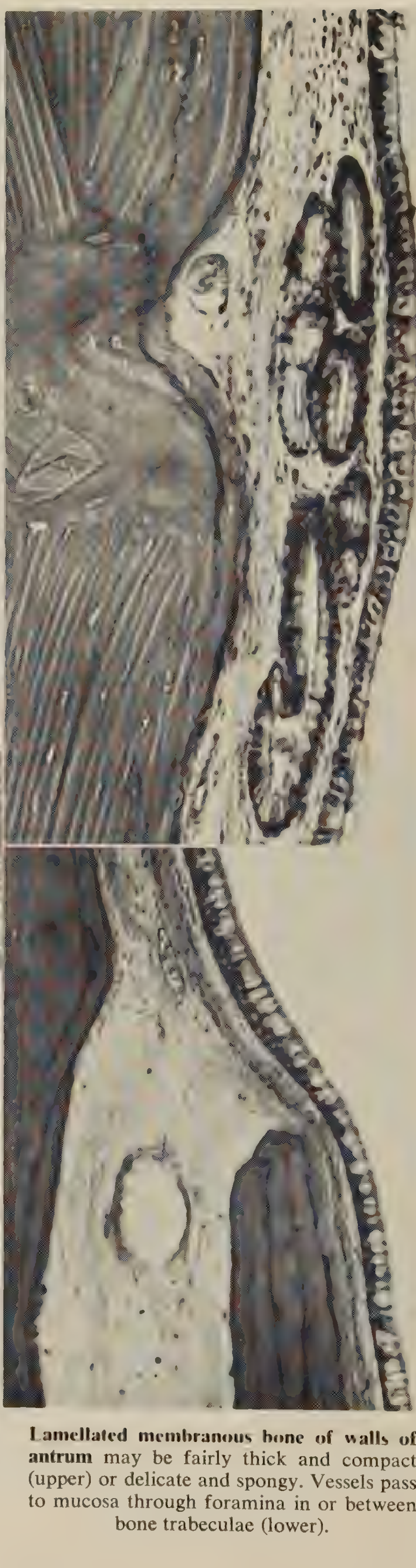

Epithelium of
Conchal Cell
Conchal
Cell
Mucosa of Conchal Cell
Mucosa of Turbinate

D. Tip of middle turbinate showing squamous metaplasia. x48. **E.** "Compression" atrophy and fibrosis of turbinal mucosa, separated by thin bone lamella from conchal cell. x62. **F.** Cell with edematous and congested stroma. x125.

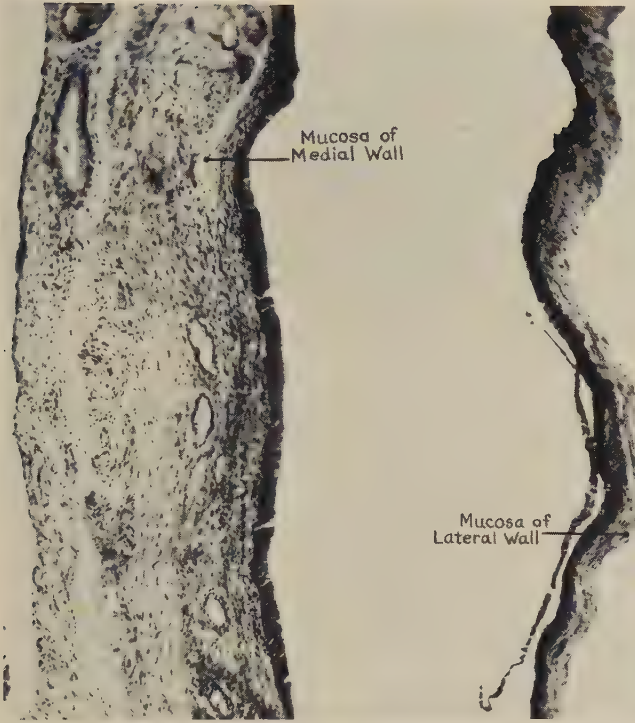
BONY WALLS OF MAXILLARY SINUS



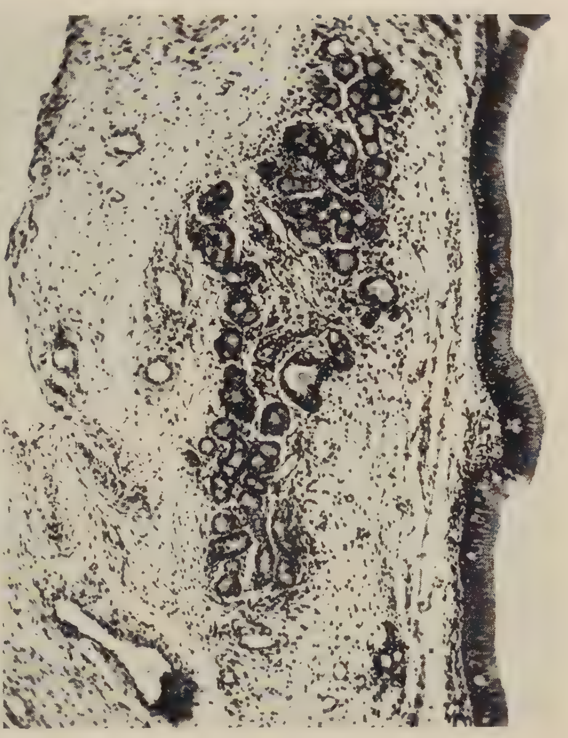
Relations of nasal accessory sinuses to each other and to neighboring structures (upper). **Floor of maxillary sinus,** extremely thin over projecting roots of molar teeth (lower) which, in some cases, perforate it.



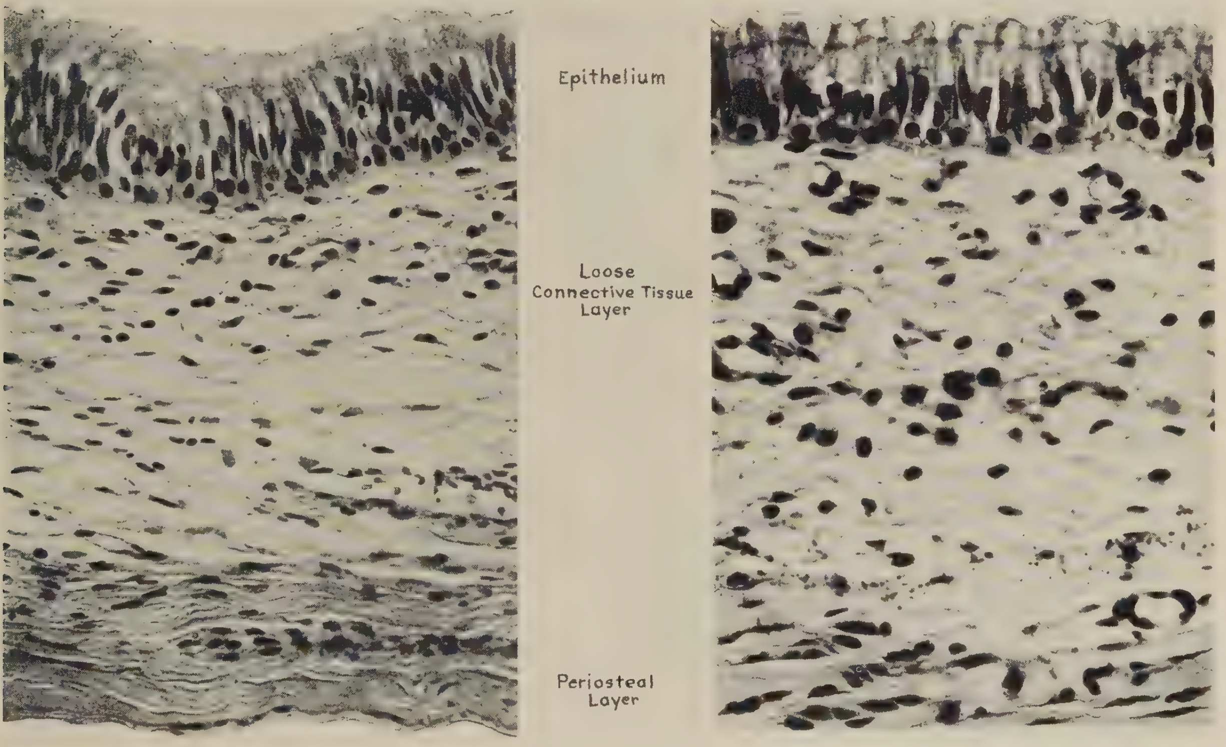
Lamellated membranous bone of walls of antrum may be fairly thick and compact (upper) or delicate and spongy. Vessels pass to mucosa through foramina in or between bone trabeculae (lower).


Mucosa of
Medial Wall
Mucosa of
Lateral Wall

Mucous membrane of maxillary sinus. Medial and lateral walls of maxillary sinus to show relative thickness—medial, 0.435 mm.: lateral, 0.079 mm. x 80. (Semenov)



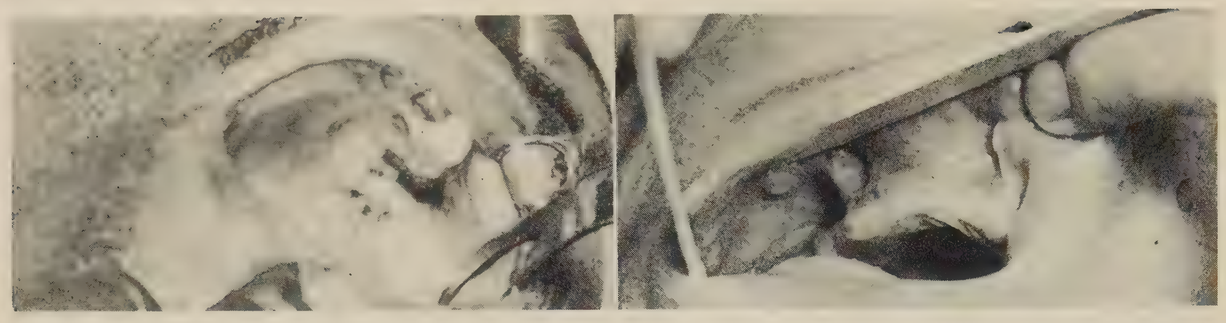
Mucosa of medial wall, particularly about the ostium, contains numerous seromucinous glands, shown in their usual location between upper loose and deep compact layers of the tunica propria.


Epithelium
Loose
Connective Tissue
Layer
Periosteal
Layer

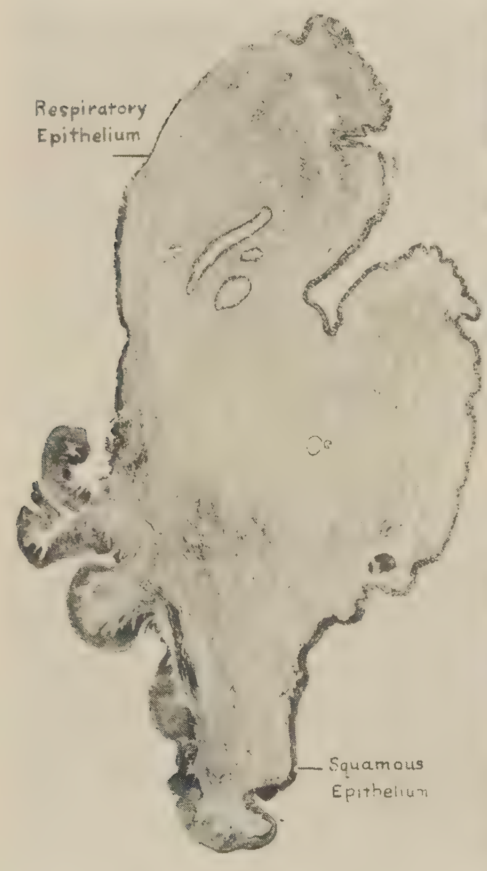
Histologic details. Ciliated pseudostratified columnar epithelium. Left: The deep compact layer of the tunica propria fuses imperceptibly with the periosteum to form a dense periosteal layer, "mucoperiosteum," which is easily "stripped" in surgical procedures. Right: this loosely fibrillar periosteal layer from a 10 year old child would "strip" with difficulty. x 300. (Semenov).

ORO-ANTRAL FISTULA

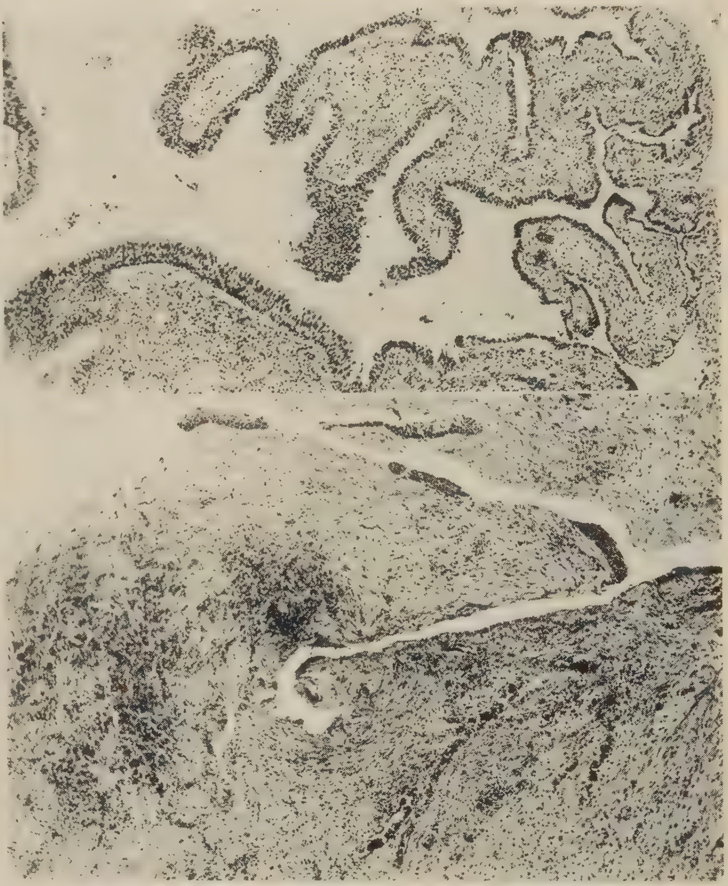
FOLLOWING TOOTH EXTRACTION



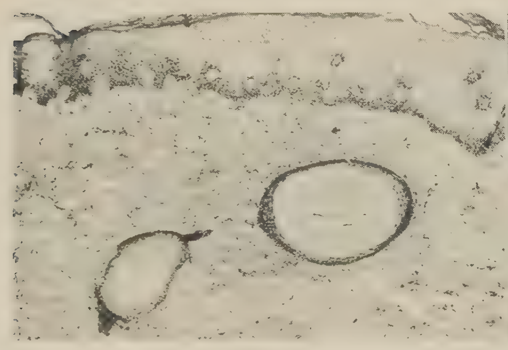
Oro-antral fistulae following extraction of molar teeth, with prolapse of antral mucosa: **A,** through ridge of alveolar process; **B,** through buccal plate of an alveolus.



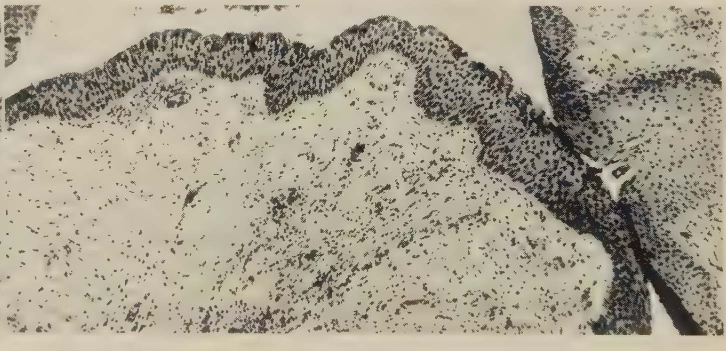
Prolapsed membrane with sinus mucosa at top, gingival mucosa at bottom. x 13.



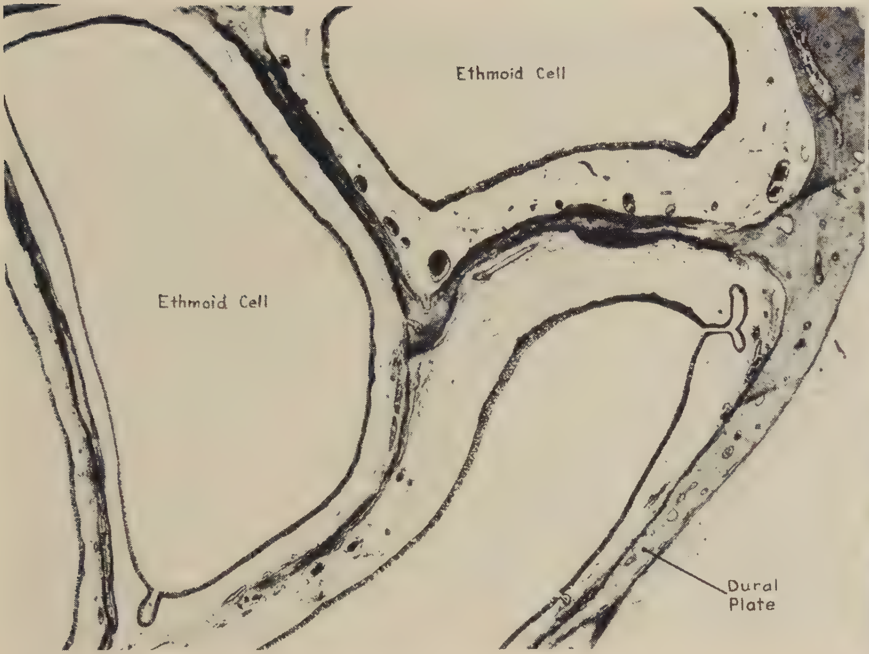
C. Polypoid hyperplasia, antral mucosa in sinus part of tract. x 62. **D. Dense scar tissue** from fistulous tract of seven months' duration. x 53.



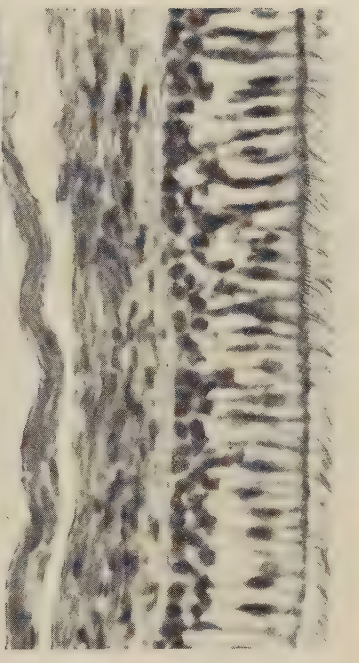
Epithelial inclusions at buccal margin of fistula. x 45.



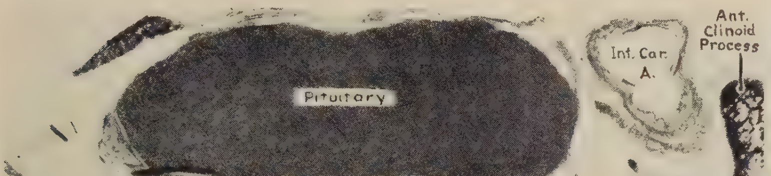
Reepithelization of scar. x 45. Modified respiratory epithelium at left, squamous epithelium at right. x 76.


Ethmoid Cell
Ethmoid Cell
Dural Plate

Ethmoid cells vary considerably in size and shape. The thin delicate mucosa is attached to very slender bone trabeculae, is well vascularized, and contains few seromucinous glands. Only an occasional simple tubular gland in this field. (Semenov).



Ethmoid mucosa. Ciliated respiratory epithelium. Thin tunica propria blends with periosteum. x 500.


Ant. Clinoid Process
Int. Car. A.
Pituitary
Int. Carotid A.
Cavernous Sinus
Internal Carotid Artery
Intersinal Septum

Sphenoid sinuses, asymmetrical, with the usual lateral displacement of septum. Delicate mucosa lacking glands remains adherent to sinus on right only. Coronol section through body of sphenoid, pituitary, and portions of contents and carotid groove. (W. Mueller, Boston).

Sphenoid mucosa, characteristically wrinkled after "stripping." Ciliated respiratory epithelium; loose subepithelial fibrous tissue; denser periosteal layer. x 75.

CHAPTER 14

RHINITIS AND SINUSITIS

While there are structural, histologic, and physiologic differences that modify reactions in the nose, paranasal sinuses, and nasopharynx, the intimate anatomic relationships and the similarities in the histology and physiology of these parts make it appropriate to consider first the general aspects of the inflammations of these structures. As shown in the section on histology, the first two are lined by the same type of epithelium—the ciliated, pseudostratified, columnar, schneiderian mucosa, except for the significantly specialized olfactory portion in the vault of the nose, and the nasopharynx which is lined by lymphoepithelium.

The mucosa of the nose is modified by the richly vascular, erectile subepithelial stroma, most prominently over the lower and middle turbinates. The nasopharyngeal mucosa on the other hand is characterized by the presence of lymphatic tissue as a diffuse component and as focal nodules that constitute the adenoids and tonsils of Waldeyer's ring. The mucosa of the paranasal sinuses differs from that of the other portions of the upper respiratory tract in the absence of the lymphatic tissue elements, in the scarcity of glands, in the relative scarcity of blood vessels, and in that it is much thinner and more closely applied to the bony walls of the cavities.

The anatomic feature of the paranasal sinuses most influential in inflammations is the relatively small ostia that can be so readily occluded, thus interfering with adequate aeration and drainage. On the other hand, all infections of the nasal cavities have ready access to these openings. In addition, there are specific anatomic features in the individual sinuses that are potent influences in both the origin of inflammation and its dissemination.

Maxillary Sinus.—A striking feature is the thin barrier offered by the floor of this sinus to inflammations. The delicate lamella of cortical bone is easily penetrated by a suppurative infection in the alveolar process of the maxilla and about the maxillary molars, and it is readily fractured and perforated during extraction of these teeth. The thin nasal wall of the maxillary sinus may be penetrated by ulcerative inflammations in the nose, and these thin barriers readily permit the extension of malignant tumors from one cavity to the other, or erosion may result from pressure of expanding benign tumors.

Ethmoidal Sinus.—The bony lamellae of the cell walls are very delicate and erosions into the orbital cavity or into the anterior cranial cavity are not infrequent complications of purulent sinusitis. The ethmoids are readily invaded by tumors primary in the orbit, in the meninges, in the nose, and in the maxilla.

Sphenoidal Sinus.—Tumors and such defects as congenital craniopharyngeal fistulas may be found in this sinus. Chronic sphenoidal sinusitis resulting in osteomyelitis may involve the ethmoid, and the infection can extend into the cranial cavity, introducing the possibility of cavernous sinus thrombosis.

Frontal Sinus.—The specific factor here is the ease with which infections invade the cancellous walls of the sinus and extend into the remote portions of the frontal bone by the resulting thrombophlebitis of the diploic veins. Of serious import is the comparative readiness with which infections extend along the penetrating vessels into the cranial cavity and establish epidural and subdural abscesses—this without necessarily involving the anterior wall of the sinus.

ETIOLOGY

Age.—Inflammations of the nose and paranasal sinuses are more frequent in children and young adults than in members of the older age groups. This may be explained by the lower degree of immunity, the more frequent exposure to cold and wet, the higher incidence of childhood diseases, and the greater prevalence of allergy. The allergy may be a local one, limited to the upper respiratory mucosa, or it may be a systemic or a remote allergy that affects the vascularity of the mucosa reflexly.

Climate is an influence, particularly when there are sudden changes of temperature; but warm, comparatively stable conditions even in the tropics are not proof against upper respiratory inflammations. So-called tropical colds are frequently severe because the conditions are favorable for the propagation of bacterial infections, and chilling is still possible in the tropics. Another factor of especial importance among newcomers to the tropics is the exposure to allergens such as those of indigenous food and plants, against which there has been no opportunity to acquire immunity. On the other hand, in the really cold climates where there are not the sudden changes in temperature, where the body is usually well protected, and where infections generally are at a low ebb, upper respiratory infections are relatively uncommon. The drying effect of the average heating facilities in homes is a factor, and any constitutional disease of a debilitating nature will, of course, lower the resistance of the mucous membranes.

Structural and **acquired conditions** that interfere with the drainage and ventilation of the nose and sinuses, such as large tonsils and hypertrophied adenoid tissue, septal and turbinal deformities, including septal spurs, may predispose to infections and allergic reactions. It can be said that any factor that interferes with the integrity and composition of the mucous blanket, with the action of the epithelial cilia, or with the normal local or systemic immunologic processes may lay the groundwork for infections and allergic reactions.

The function of the sinuses is not known. Some are of the opinion that they are residual olfactory organs. With the diminution of the olfactory function in man the communications with the nasal cavity have become more and more restricted to their present small ostia that are so readily occluded by inflammation and by mechanical means. The sinuses in man share with other vestigial structures a lower vitality and a less active regenerative capacity than are offered by normally organized and functioning parts of the body. The sinus mucosa will, however, regenerate satisfactorily if conditions are favorable.

Defense Mechanism.—Bacteria that penetrate the mucous blanket and the epithelial mucosa are taken care of by the phagocytes, usually the large histiocytic or reticuloendothelial cells, and by the humoral antibodies. If these defenses fail and the bacteria are able to establish a foothold, polymorphonuclear leukocytes, attracted by positive chemotaxis, attempt to eliminate or to isolate them.

There is little doubt that subclinical chronic sinusitis is common, especially in the ethmoidal sinuses. It may remain subclinical for long periods until there is an exacerbation induced by an acute allergic reaction, polyp formation, acute infection, or trauma that interferes with drainage.

CLASSIFICATION

It is possible to divide rhinosinusitis on an etiologic basis as follows:

1. Infectious (bacterial and viral)
2. Allergic
3. Mixed

From a morphologic standpoint it is possible to differentiate at least nine types of reaction as follows:

Catarrhal	Usually acute
Ulcerative	
Hemorrhagic	
Hyperplastic	Chronic
Polypoid	
Fibrous	
Cystic	
Follicular	
Papillary	

The terms **hemorrhagic, ulcerative,** and **polypoid,** are self descriptive.

The **hyperplastic** form shows abundant exudate, chiefly plasma cells, invasion of fibroblastic and reticulum cells, and increase in young blood vessels.

The **fibrous** reaction includes very little exudate, but much fibrosis (scarring) of the stroma, a decrease in vascular elements and possibly also in the number of glands. This form might also be termed atrophic.

The **cystic** form is of two types:

A. Glandular — retention cysts of gland elements.
B. Interstitial (pseudocystic) lakes of edema in the stroma and lymphangiectasis.

The **follicular** type is so called because of the presence in the mucosa of secondary lymphatic nodules.

The **papillary** form is usually associated with the hyperplastic reaction in which superficial edema and exudate form gross or microscopic papillary thickenings in the mucosa. This must not be confused with the papilliferous architecture frequently taken by frank carcinomas, especially those of the paranasal sinuses.

Such a detailed classification is of interest, however, chiefly to the morphologist and perhaps has little practical value because a number of the forms are simply stages in the progress of inflammation to organization and scarring.

In an analysis of 150 cases in the Registry of Otolaryngic Pathology at the Armed Forces Institute of Pathology it was found that in instances in which allergy was an etiologic factor, the tissues tended to be of the polypoid and fibrous types; that ulceration and hemorrhage were the results of pyogenic infection or trauma, and that the hyperplastic type of reaction occurred most frequently in the infectious group.

One striking feature in all except those with ulceration was the scarcity of the suppurative type of exudate in the mucosal stroma, even when the discharges were mucopurulent. This leads to speculation on the part played by bacteria, which may, as Fenton, Semenov, Holmes and others have contended, be minor in comparison with the less tangible factors of environment, vasomotor sensitiveness, emotional instability, and diet, in the general run of cases.

In 25 per cent of the 150 cases reviewed frank secondary lymphatic follicles were present. This is not a novel feature, for they occur commonly in chronic inflammations in a wide variety of situations where lymphatic tissue is not normally present. The development of these follicles can be clearly traced. They begin as a collection of lymphocytes about a blood vessel. This collection concentrates, the vessel "moves" to the periphery of the mass, and finally a so-called germinal center appears and reticulin fibers develop. These follicles were not common in the pure allergic cases, but were frequent in those of mixed etiology. It has been stated that these follicles are common in the deeper portions of the stroma near the periosteum. It is our experience, however, that they are predominantly in the upper layers, many of them in direct contact with the epithelium. In fact, they may cause papillations or extrude into the cavity, especially in severe chronic inflammations. Care must be exercised to differentiate such prominent lymphatic-tissue components from the infiltrations of leukemia.

A striking feature in the picture of the chronically inflamed membrane is the enormous amount of reticulin in the stroma. In addition to the concentration in the basement membrane that results in the thick, glassy subepithelial structure, a network can be demonstrated in silver preparations, generally distributed throughout the stroma in close association with the reticuloendothelial cells. This reticulum-cell activity is responsible for much of the ultimate density of the mucosa, which is caused in part by collagen from the fibrous tissue proliferation.

The thick basement membrane has been interpreted by some as part of the defense mechanism of the tissue. This seems dubious because adequate reepithelization of such a physiologically inactive structure is scarcely possible. More probably it is evidence of the too exuberant attempt to repair the damage of the inflammation.

Another feature more prominent in the polypoid type of reaction than in the scarring form is the development of pseudoglands by the invagination of the surface epithelium and its metaplasia to the glandular, secreting type. These pseudoglands can reach considerable size through occlusion of their orifices, appearing as mucin-filled cysts or, in the presence of infection, microabscesses.

CLINICAL TYPES

The lining of the nose, paranasal sinuses and nasopharynx, being mucous in type, is susceptible to the comparatively simple reaction, **catarrhal inflammation.** This consists of edema of the stroma, increased mucus secretion by the glands and by such goblet cells as are present in the surface epithelium, but of a minimal cellular exudate consisting chiefly of lymphocytes and plasma cells rather than polymorphonuclear leukocytes. Catarrhal inflammation is a benign and acute type of reaction and does not lead to the complicated organization and repair processes that are inevitable in suppurative and granulomatous inflammations. It results from infections of low virulence. It is characterized clinically by a serous or mucous discharge and a pale or bluish mucosa thickened by edema and congestion.

An excess of mucus is not limited to catarrhal inflammation. Some mucus is normally elaborated by the epithelium of the sinuses, but when a great deal of thick mucus is formed, it usually indicates the presence of inflammation, particularly of the chronic allergic type, associated with some degree of hyperplasia or polypoid thickening of the mucosa. When an occasional mucus-forming cell is present it may assume a typical "goblet cell" appearance, but when large numbers of ciliated columnar cells undergo mucinous conversion the typical cellular outlines are not apparent. The surface of the epithelium merges with the mass of mucus and many epithelial cells may be desquamated. A considerable area of epithelium can be affected so severely that only a layer or two of cuboidal basal cells remain behind. These basal cells give rise to new ciliated columnar epithelium, but the exact manner and rate of regeneration is not certain.

Acute rhinitis—the common cold—is usually a self-limiting inflammation of the mucosa, frequently involving the paranasal sinuses. It has been established that this is a viral disease which confers, at best, a temporary immunity and which is practically always complicated by bacterial infection. Involvement commonly extends not only to the sinuses but to the pharynx and the lower respiratory tract as well.

The pathogenesis is interference with the vasoconstrictor mechanism that produces hyperemia and exudation, with exfoliation of the epithelium. The exudate in the early stages is serous in nature and abundant in quantity. Later it becomes mucopurulent or purulent, depending on the character of the complicating bacterial infection. In treatment, it is necessary to avoid agents such as silver nitrate, water, or undue trauma that interfere with the normal ciliary activity and the integrity of the mucous blanket.

Acute sinusitis may be catarrhal or suppurative. It appears microscopically as edema, infiltration of polymorphonuclear and mononuclear cells, minute hemorrhages, areas of ulceration or desquamation of epithelial cells, and marked engorgement of the blood vessels. The surface of the mucosa is red, covered with yellow pus or mucopus that is composed of mucus, bacteria, pus cells, and desquamated epithelium.

Allergic Rhinosinusitis.—The abundant and physiologically specific vascularity of the nasal mucosa is an important factor in localization of the allergic reaction in its uncomplicated form in the upper respiratory tract. This is largely a vasomotor phenomenon characterized by vascular dilatation, edema, and a cellular exudate rich in eosinophils. While the allergic reaction is predominantly local due to local sensitization and to local exciting factors, it may be a localized reaction to a more remote allergy such as ingested food to which the patient is sensitive. In its pure form it is an evanescent reaction, but it becomes serious in the upper respiratory tract because, first, it is frequently complicated by secondary infection and, second, the persistence of the basic sensitivity leads to a chronically recurring condition. Both of these factors result in sustained and chronic changes that can become irreversible.

There are unfortunate interrelationships between allergies and infections. The former facilitate the establishment of infections and, conversely, specific sensitization to bacteria may be produced by the infections. As a rule, however, infection is not a problem in the rhinitis of hay fever.

It is evident that in addition to the specific sensitivity, there must be underlying constitutional factors leading to the establishment of the allergic state, because all individuals do not experience the difficulty and there is a wide variation in the exciting factors in those that do. The allergic, or hyperergic state, as it is sometimes called, is not too clearly understood. It may be due to a sensitization of cells because of inherent constitution or previous exposure to an allergen. As a result of this sensitization, the cell reacts violently to re-exposure to that antigen. The cell may be destroyed, but an essential feature seems to be the liberation of histamine, the really potent factor in the clinicopathologic reaction. Or it may be explained on the basis of the reaction between the antibodies present in the body fluids and the specific antigen. This combination produces a toxin, which in turn influences the clinicopathologic picture. It has been shown experimentally that the picture of vasomotor rhinitis can be simulated following severance of the cervical sympathetic nerve trunk or its injection with novocain (Fowler).

Jensen considers that many of the nose and throat complexes, particularly in children, are on an allergic basis, and that not enough attention has been paid to this fact by those who have treated children for repeated colds and inflammations of the upper respiratory tract. Lymphoid hyperplasia is a typical symptom in allergic states, and regrowth of tissue after adenoidectomy is particularly common. In 44 patients with polyps, he elicited a history of allergy in 42.2 per cent and histologic evidence of it in 41.6 per cent.

Allergy can produce profound changes in the appearance, structure, and function of the mucosa. It alters the character of the mucous blanket and limits ciliary activity. The epithelial impingement on contiguous structures by congestion of both blood and lymph vessels, edema, or polyps interferes with ventilation and drainage of the nasal and sinus cavities, favoring infection and further deterioration of the mucosa. Allergic rhinitis and sinusitis often exist together but may appear separately.

In typical allergy the discharge is gray and mucinous, the smears contain eosinophils, and radiographs show the fuzzy partitions of bilateral hyperplastic pansinusitis. In mild cases the sinusitis may be latent and asymptomatic. It is only when all symptoms and signs are typical that one can be certain of the diagnosis of allergy. A far greater number of cases exist in which the picture is atypical. They belong to the variations of sinusitis which for want of a better name are known as borderline allergies, mixed allergies and infections, or equivocal cases.

Histologically, the uncomplicated reaction in the respiratory mucosa is edema of the stroma, which in the active phases may appear and disappear rapidly, and cellular exudate particularly rich in eosinophils. The percentage of eosinophils varies with the stage and with the intensity of the reaction. A count in excess of 20 per cent in the tissues or secretions has been arbitrarily fixed as a criterion of the allergic reaction. With the advent of bacterial infection the exudate will include polymorphonuclear leukocytes. With the subsidence of allergic reaction the edema lessens or disappears and the percentage of eosinophils decreases.

In chronic allergic sinusitis the epithelium shows marked mucinous degeneration and desquamation. A certain amount of reaction is sustained by bacterial complication. With each recrudescence of the allergic reaction there is an accentuation of the edematous feature, a rise in the proportion of eosinophils, and the introduction of reparative processes—new blood vessel formation and fibroblastic proliferation. Particularly important is the reticuloendothelial proliferation that leads to the accumulation of more and more intercellular reticulin, particularly in the subepithelial basement membrane. The development of the thick basement membrane can be traced by silver impregnation techniques. In the early stages fine fibrils can be seen in contact with well preserved reticuloendothelial cells. As the process progresses and the amount of fibrillar content increases, the intercellular fibrils become thicker and thicker by fusion and hyalinization and the enmeshed reticuloendothelial cells are reduced in number by pressure atrophy.

The accumulation of fluid in the stroma may be sufficient to produce the polypoid state. When this accumulation is focal a vicious cycle becomes established, consisting of enlargement, restriction of drainage of fluid, and some interference with blood supply. A pendulous mass—the clinical polyp—results. The fluid may accumulate in interstitial spaces in sufficient quantity to form grossly detectable cysts. Pathologically these are pseudocysts without cellular lining.

In the allergic reaction the mucous glands play a subsidiary role. They may be hypersecretive in acute cases, but in the chronic state they suffer from the accumulation of large amounts of exudate around them or by the subsequent fibrosis. At times the ducts are occluded, either by exudate or by fibrosis, and retention cysts result. These are true glandular cysts lined by epithelium, a feature distinguishing them from the pseudocysts. Cysts of both types may reach macroscopic size.

Clinically, the allergic reactions of the respiratory tract are divisible into three groups. The first is the HAY FEVER group in which the sensitization is to the pollens of early spring, early summer and fall. This form of allergy causes the most intense of the acute reactions. It is characterized by profuse serous exudate with alternate swellings and contractions of the nasal mucosa. The exudate may later become more mucoid or even purulent. The conjunctival mucosa usually participates in the reaction.

The second form is PERENNIAL ALLERGIC RHINITIS (synonyms: vasomotor rhinitis, atopic coryza). This is a more continuous reaction without the periodicity of the hay-fever type, because exposure to the exciting factor, such as house dust, feathers, powders used in cosmetics, and food and drug allergens, is constant. This group includes, therefore, reactions not only to the allergens that are present locally as inhalants, but also those that are ingested, and in addition the very important but less sharply defined bacterial sensitization that results from infections of the nose, sinuses, and tonsils. It is this form of rhinitis that is more likely to develop chronic phases, evidenced by polypoid, hyperplastic, follicular and fibrotic mucosae. Bacterial allergy is no doubt responsible for a considerable percentage of the nasal reactions. A rarer group is that which results from sensitization to physical agents, such as light, heat, and cold.

The third clinical manifestation of the allergic state is ASTHMA. This is of two types, extrinsic and intrinsic. The first can be traced to specific allergens, but the second is not so sharply defined and may be of bacterial origin, sometimes based on infected tonsils or sinuses. It is very likely that hereditary hypersensitivity is also a factor. The mechanism of the paroxysms is not clearly understood. The clinical picture is the result of spasm of the musculature of the bronchioles and smaller bronchi and hypersecretion; together these cause difficulty in expiration and, to a smaller degree, in inspiration. The pathology of asthma is discussed in greater detail in the section on the lungs.

The allergic state also manifests itself in the respiratory tract as local urticaria. This is a transient state leaving no residuum. It involves patches of the nasal mucosa, epiglottis, or larynx. In the last instance it may be of sufficient proportions to lead to suffocation. This type of reaction is seen occasionally in the early stages of influenza and the common cold.

Incidence of Allergy.—Semenov's criteria for the determination of allergy are the history of hay fever or asthma, a typical, pale bluish appearance of the turbinates, polypoid changes in the mucosa and hyaline degeneration of the basement membrane, mucoid degeneration of the epithelium, and tissue eosinophilia. At times identification of an allergic process is difficult. Over five hundred specimens examined by Semenov showed histologic evidence of an underlying allergy. Seventy-two per cent of the cases showed a purulent factor, either alone or complicating allergy. The hyperplastic, polypoid, and cystic nonpurulent forms made up the remaining 28 per cent. The incidence of cysts and abscesses is greater in the polypoid mucosa. In 80 per cent of the chronic cases streptococci were demonstrated, usually mixed with other bacteria.

Polyps do not necessarily indicate an allergic state. Those that are on that basis are usually multiple and bilateral, but the non-allergic polyps are usually unilateral and their removal is followed by better results than is that of allergic polyps.

Semenov has written in detail on the subject of allergic rhinosinusitis. We are indebted to him for the use of a number of illustrations in this section.

Infectious Rhinosinusitis. — Normally present in the upper respiratory tract are a wide variety of pathogenic bacteria — streptococci, staphylococci, pneumococci, and very rarely the organisms of Vincent's disease—ready to take advantage of any breakdown in the protective mechanism. Certain of the organisms, in addition to the diphtheria bacillus, are capable of stimulating the diphtheritic type of reaction which includes the development of a pseudomembrane. This membrane is made up of a framework of fibrin that enmeshes cellular exudate and bacteria. Streptococci and particularly pneumococci cause this type of reaction.

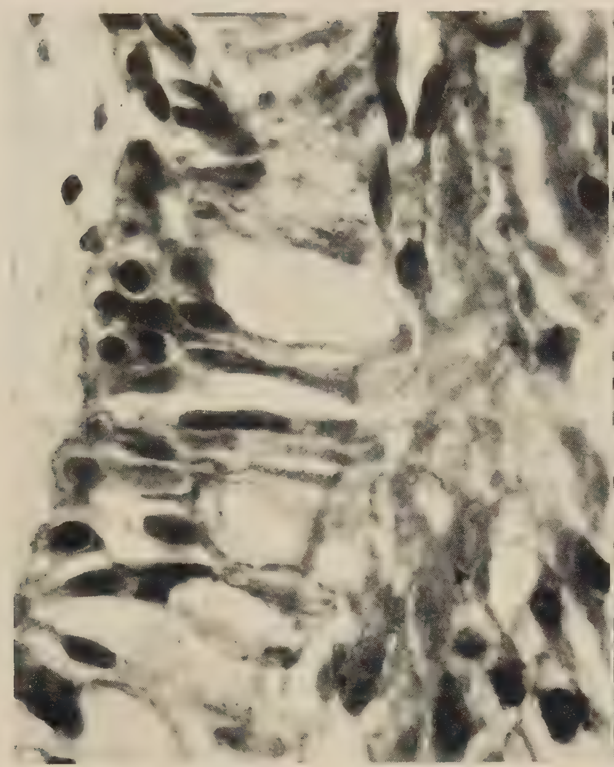
Chronic Vasomotor Rhinitis (other than that of strictly allergic and infectious origin).—Emotional and other stressful disturbances, the vasomotor instability at puberty and during pregnancy, and hypothyroidism have been mentioned as causative factors. Anatomic alterations in structure, such as chronically enlarged turbinates and adenoids, can be the underlying cause or may themselves be allergic in origin. Marked deviation of the septum to one side can also be responsible, as it creates a compensatory hypertrophy of the mucosa of the middle and inferior turbinates on the opposite side that interferes with the adequate drainage of the nasal cavities. Irritating dusts and the indiscriminate use of nasal medication appear responsible for some cases. As a matter of fact, however, it has been found that the majority of cases are on an allergic basis or result from chronically infected sinuses, most commonly the ethmoid, or from repeated and prolonged attacks of acute infection.

Microscopically, there is chronic engorgement of the blood vessels, especially of the cavernous plexuses of the turbinates, and hypersecretion of the mucous glands in all forms of chronic rhinitis. In the hyperplastic form the submucosa is thickened and the number of fibroblasts is increased. Edema is associated with dilatation of the blood vessels and of the cavernous plexuses, and the smooth muscle of the deeper vessels shows foci of hypertrophy as well as of atrophy. The periosteum thickens and the epithelium shows stratified hyperplasia.

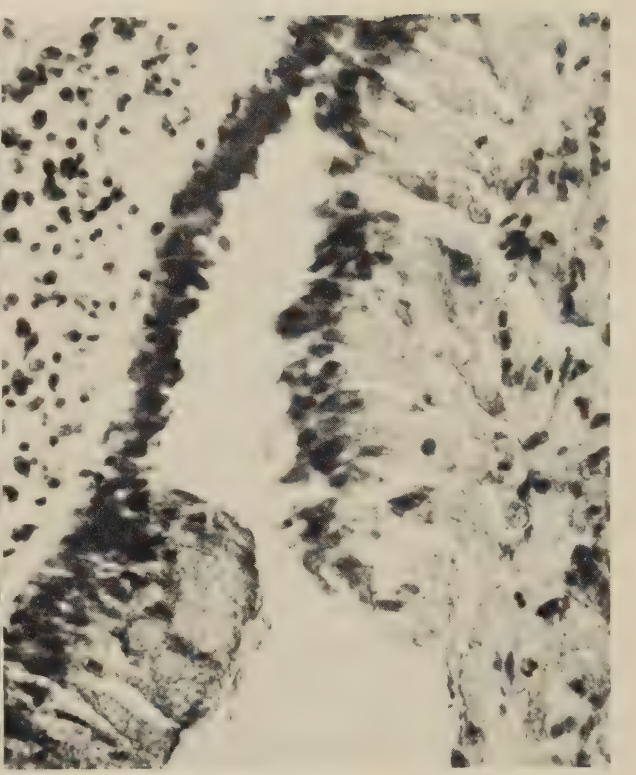
Hyperplastic rhinitis is commonly seen around the anterior and posterior ends and lower borders of the inferior turbinate, around the entire middle turbinate, and in the ethmoidal region (hyperplastic ethmoiditis). Spraying with astringents produces blanching and only slight shrinkage. Because of the exudate and the increase in fibrous tissue, focal swellings do not resolve.

Papillary hypertrophy is most common on the posterior ends and lower borders of the inferior and middle turbinates. It appears in the postnasal mirror as a pale gray or purple-red mulberry thickening due to polypoid edema, fibrosed submucosa, and especially infoldings of the epithelium (Semenov). Subepithelial diffuse and focal infiltration of lymphocytes and plasma cells occurs in nonspecific cases, and eosinophils and edema predominate when allergy is involved. The secretion is thick, sticky, gray or turbid mucus that accumulates in the middle meatus and on the floor of the nose or hangs into the nasopharynx.

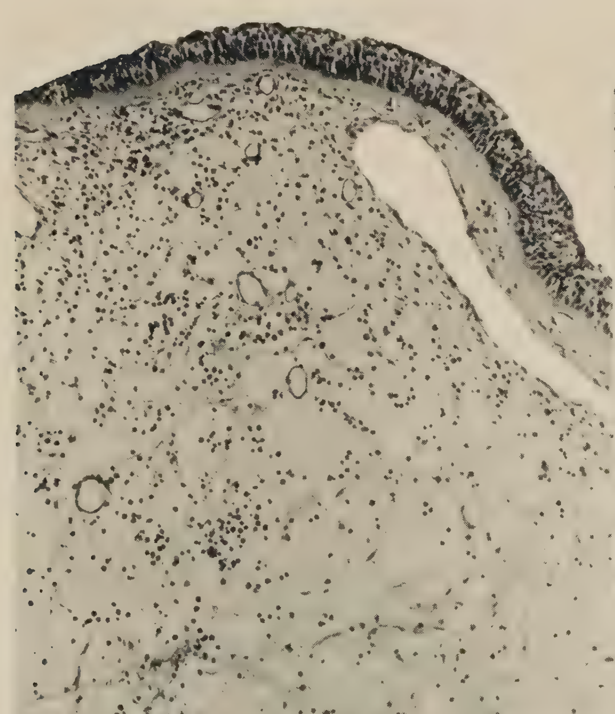
Chronic allergic rhinitis, with or without other manifestations of allergy, is frequent and differs from the hypertrophic and hyperplastic types of nonallergic or combined rhinitis in that it produces more swelling, mucus, edema, polypoid deformity, and cellular infiltration, especially of eosinophils. The diagnosis is a simple problem when there are characteristically pale, wet, boggy mucous membranes, hypersecretion, thickened basement membrane, edema, and eosinophilia. The atypical forms, borderline allergic rhinitis, are less distinctive, and sometimes cannot be classified beyond the catarrhal, hypertrophic, or hyperplastic categories common to chronic rhinitis in general.



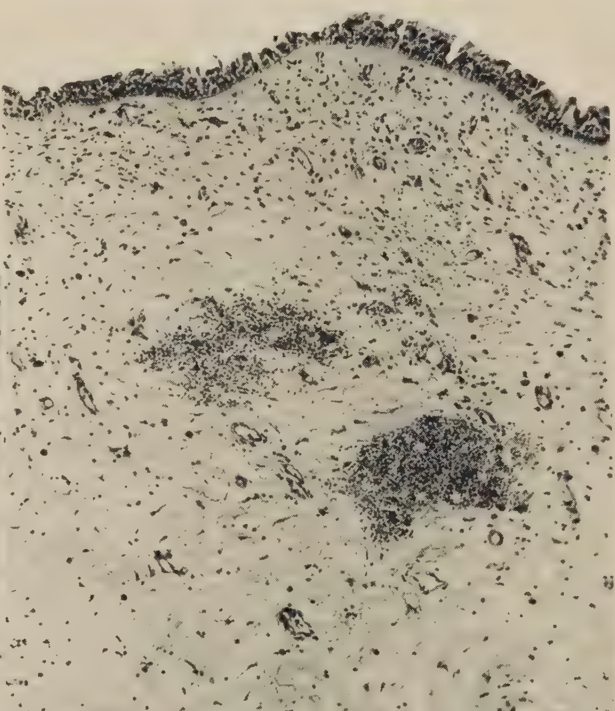
Acute catarrhal rhinitis. Increased number of goblet cells; visible cilia, some agglutinated; thick mucous blanket. x 800. (Semenov).



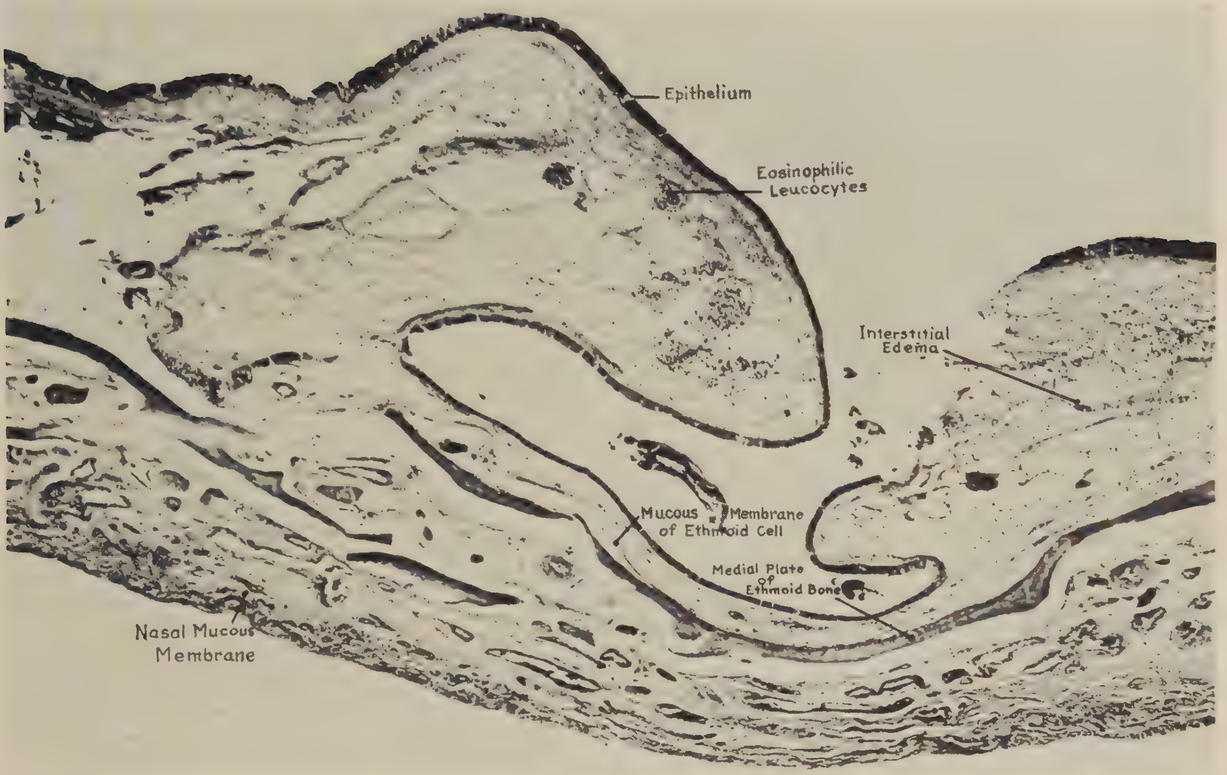
Allergic sinusitis. Mucinous degeneration and desquamation of epithelium, leaving basal layer attached to thickened basement membrane. Secretion at right. x 600. (Semenov).



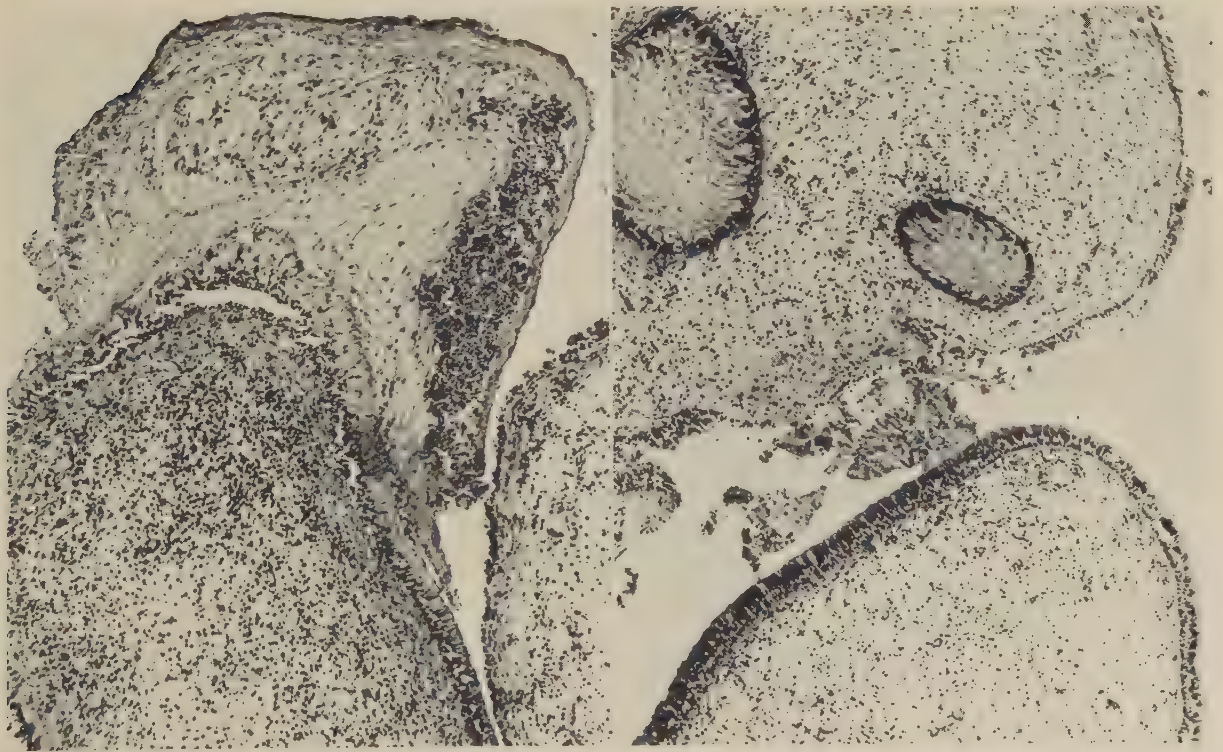
Allergic rhinitis, early polypoid. Epithelium is altered and has lost cilia; stroma is edematous and contains a predominantly eosinophilic exudate; dilated lymphatics or veins. x 120.



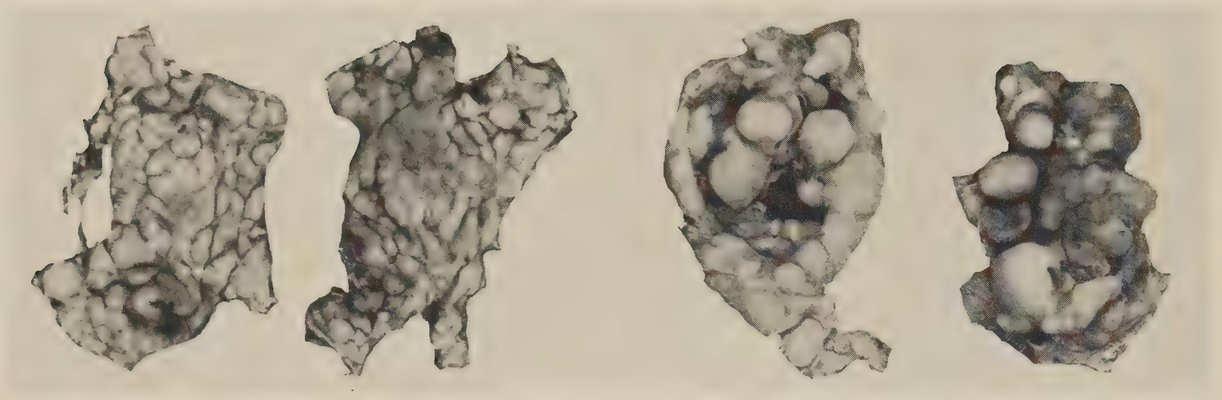
Subacute, hyperplastic, polypoid rhinitis. Less edema and exudate, but increase in fibroblasts. Small, focal hemorrhages. x 90.


Epithelium
Eosinophilic Leucocytes
Interstitial Edema
Mucous Membrane of Ethmoid Cell
Medial Plate of Ethmoid Bone
Nasal Mucous Membrane

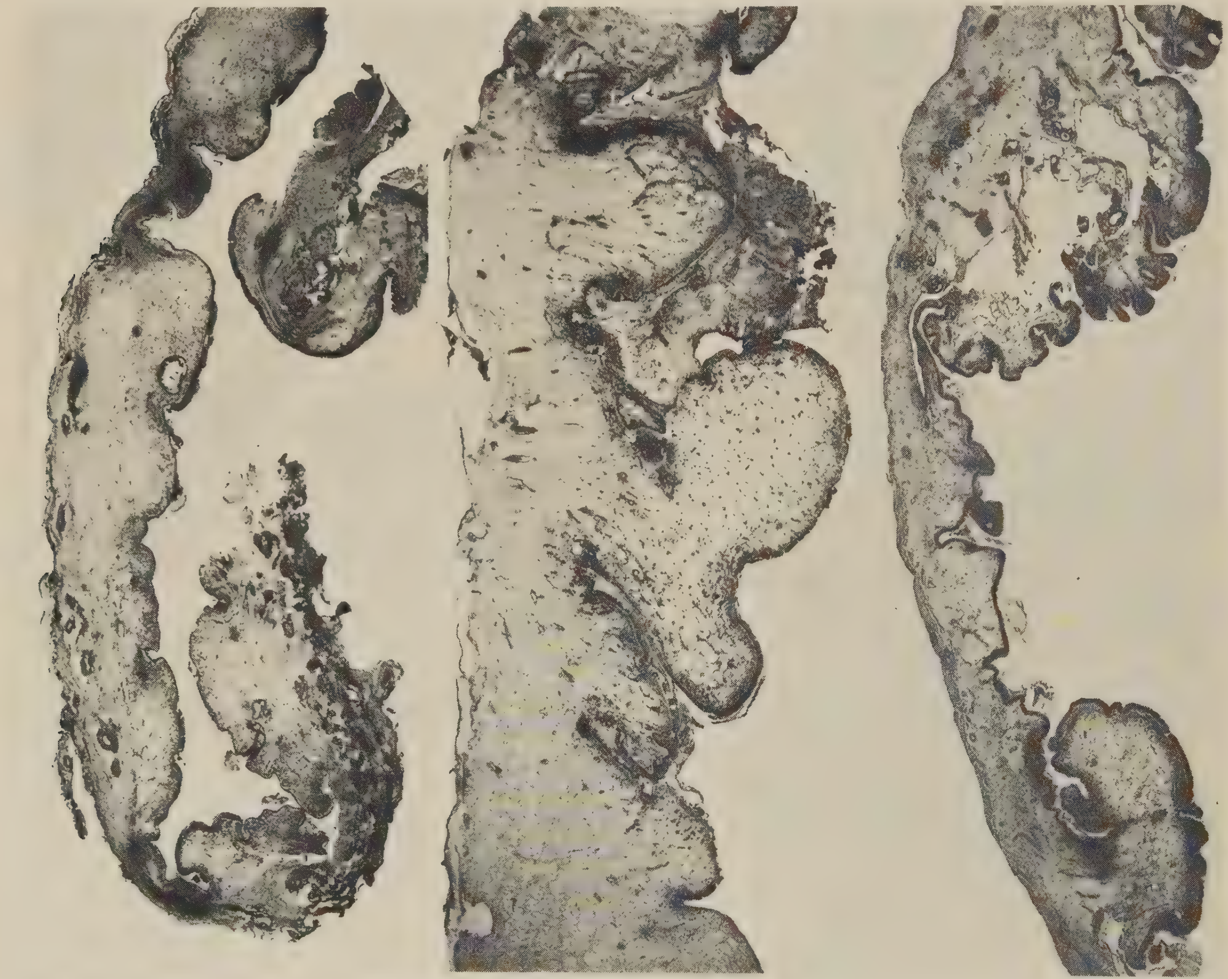
Hyperplastic sinusitis, allergic. Part of ethmoid cell in lateral wall of nasal cavity. Mucosa at center is relatively normal, but adjacent polypoid areas show marked stromal edema with distention and rupture of connective tissue fibers and infiltration by eosinophils. x 20.



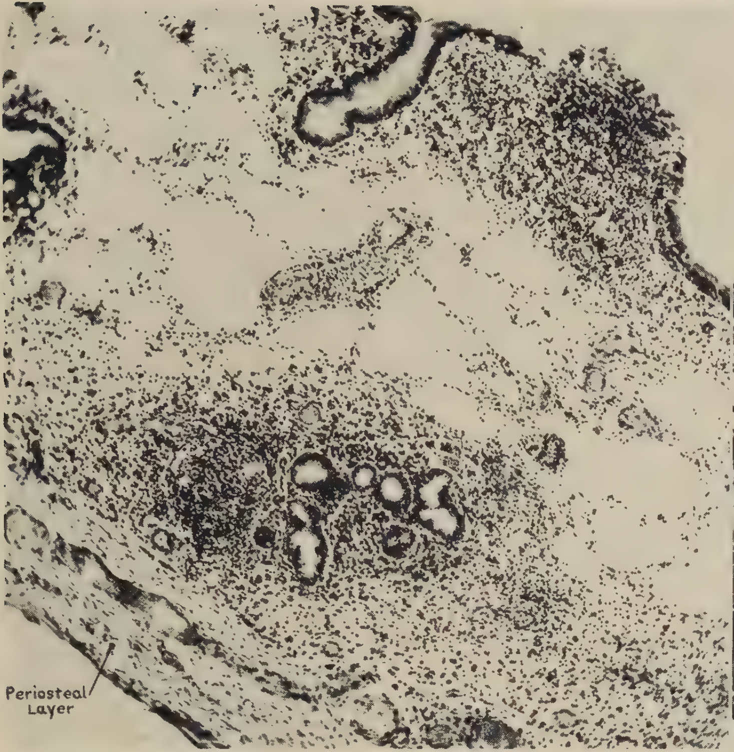
Hyperplastic rhinitis, allergic. A. "Cap" of mucus, containing masses of eosinophils, on surface of edematous polypoid mucosa. Epithelium shows transformation to mucous cell type and early desquamation. x 76. **B.** Marked interstitial edema and exclusively eosinophilic exudate. "Cystic" dilatation of two glands (at top) resulting from accumulated secretion. Thickened basement membrane. Part of epithelium shows desquamation to basal layer of cells. x 83.



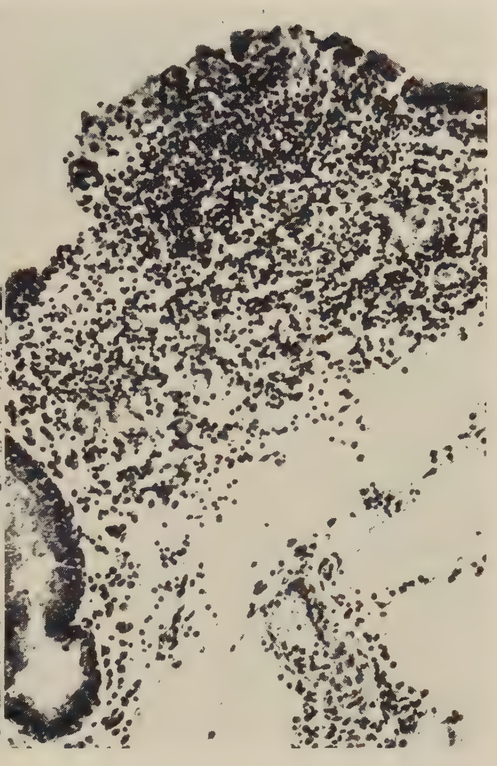
Mucous membranes of maxillary sinus surgically "stripped," in two cases of bilateral hyperplastic polypoid sinusitis of allergic etiology: *left,* uncomplicated; *right,* with superimposed infection. Small abscesses and purulent exudate in portions of polypoid "cystic" mucosa. (Semenov.)



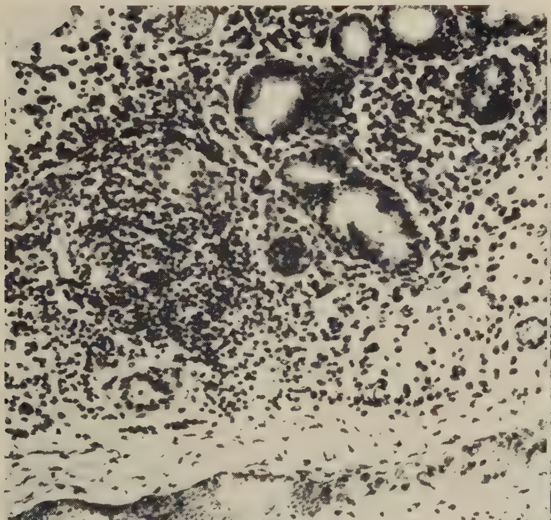
Histologic features of chronic hyperplastic maxillary sinusitis. A. Uniformly hyperplastic mucosa. Etiology uncertain. **B.** Pronounced polypoid hyperplasia due to allergy. Extensive mucus production above; edema most marked in upper parts of tunica; dense subepithelial eosinophilic exudate. **C.** Chronic suppurative polypoid sinusitis, due to pyogenic infection, produced a mucopurulent secretion. Diffuse and subepithelial concentrations of exudate, chiefly lymphocytic but containing numerous polymorphonuclear leukocytes. (Semenov.)



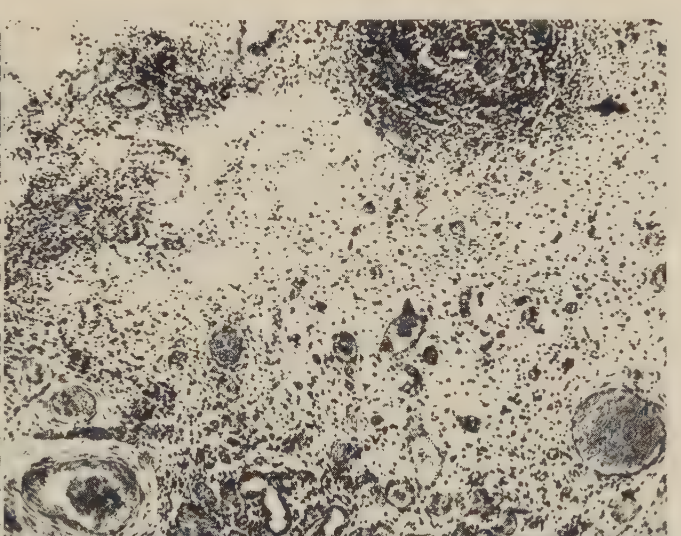
Chronic suppurative sinusitis:
Loose edematous stroma; periductal and periacinar exudate of lymphocytes, plasma cells, and polymorphonuclear leukocytes; periphlebitis (above center). Small mucosal ulceration. The periosteal layer is intact. (Semenov).



Exudate, chiefly mononuclear, but including numerous polymorphonuclear leukocytes, at site of ulceration and about vein. Edematous interstitial spaces. (Semenov).

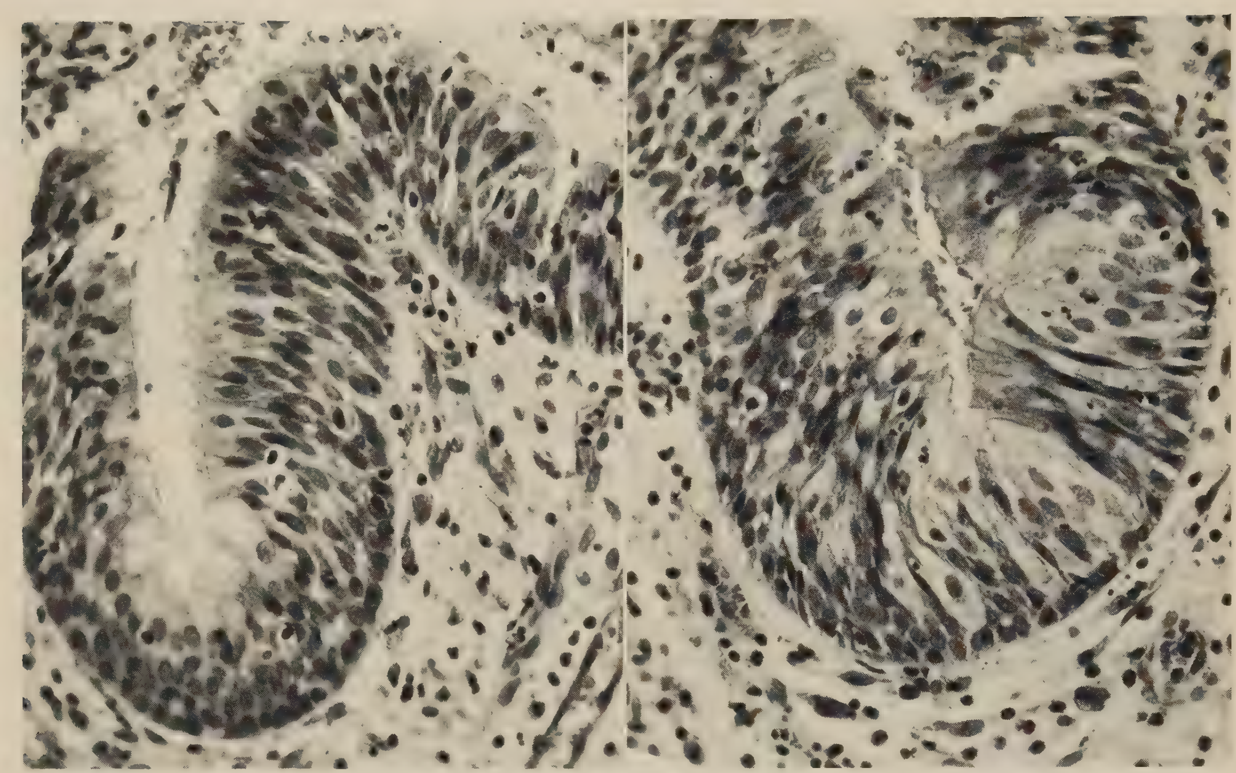


Atrophy of glands and periacinar exudate, predominantly mononuclear. Periosteal layer is congested, but free of exudate. (Semenov).

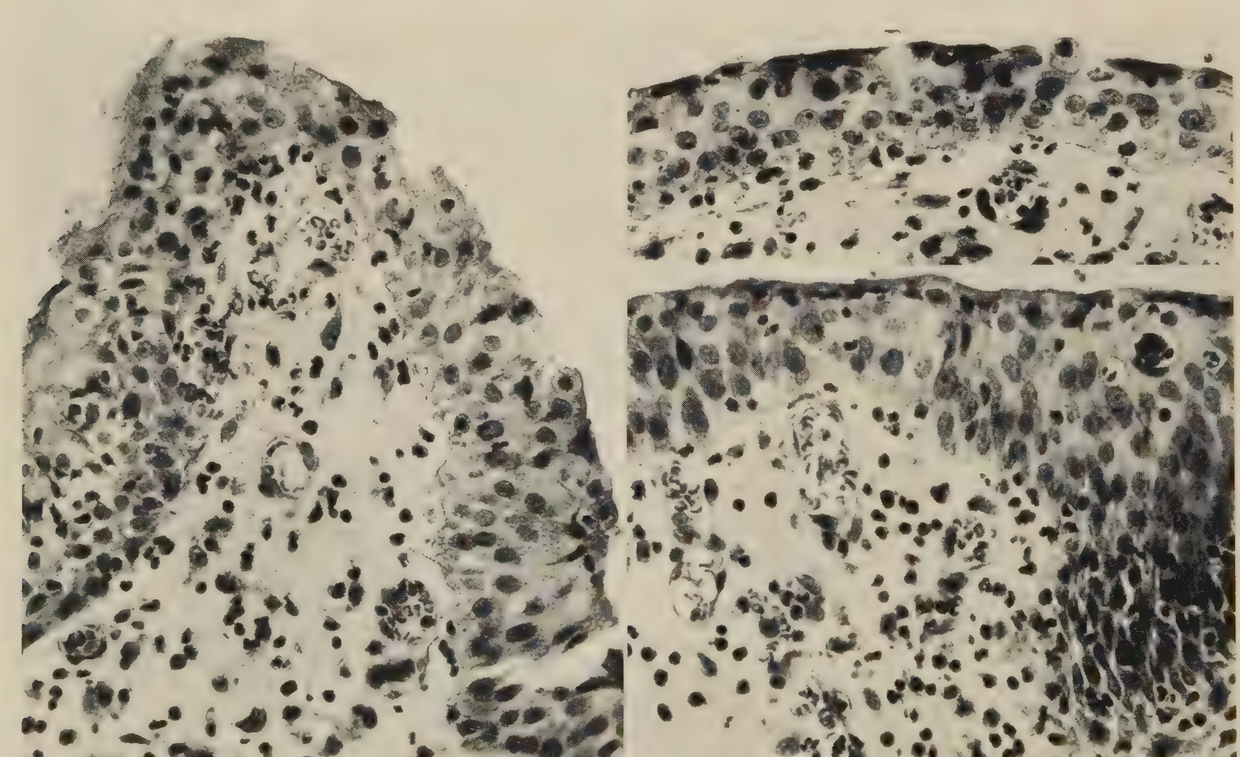


Thickened periosteal layer relatively uninvolved, sharply limits inflammatory process and is barrier to extension. Note vascular congestion; lymph follicle; prominent cellular exudate. (Semenov).

EPITHELIAL CHANGES

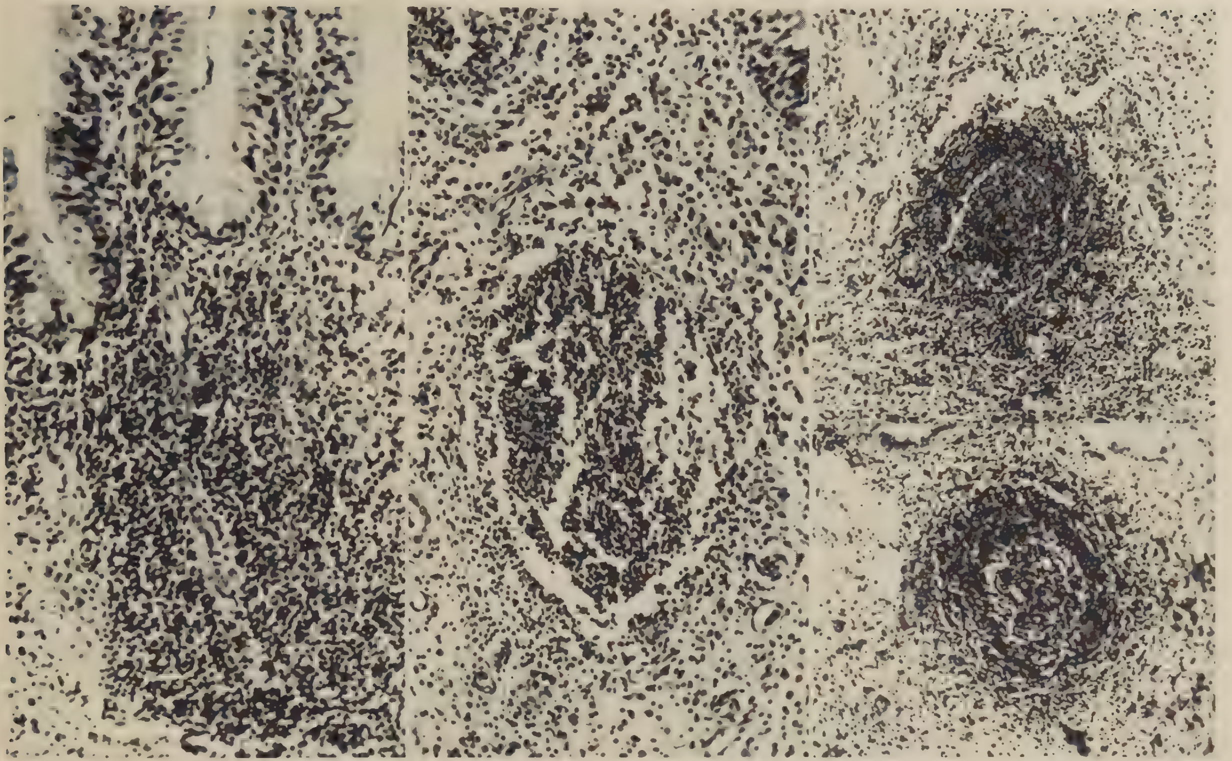


Hyperplasia of epithelium and exaggerated stratification of nuclei. A. The cilia are agglutinated and absent in some areas. B. The cells have lost their cilia; some show squamatoid character with large nuclei. A few leukocytes are migrating through the epithelial mucosa. (Semenov).

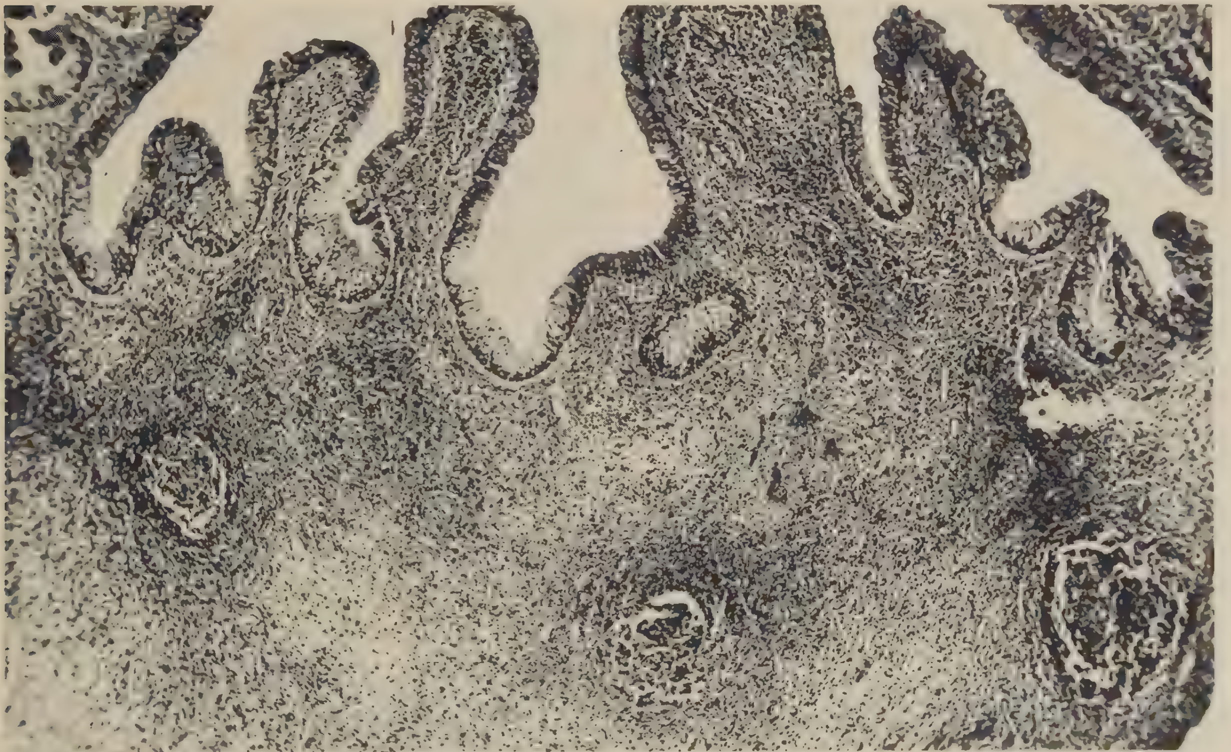


Metaplasia. The epithelium has lost its cilia, there are no goblet cells and the cells are of intermediate forms. Frank squamous metaplasia is much less frequent in sinuses than in nose. (Semenov).

DEVELOPMENT OF LYMPHATIC FOLLICLE



Development of a lymphatic follicle in the mucosa. A. **Accumulation of lymphocytes** about a blood vessel. x 145. B. **Well circumscribed collection** and free of the blood vessel. C. By further concentration it becomes a **primary follicle** such as is seen in young lymph nodes. x 125. D. Finally a "germinal" center develops and it is now a **mature secondary follicle.** x 125.



Follicles in various stages of development. Mucosa of hyperplastic maxillary sinusitis of several years duration. The surface has a papillary architecture, the stroma is thickened by fibrosis and dense mononuclear infiltrate. x 55.

CHAPTER 15

SINUSITIS

A discussion of sinusitis *per se* requires repetition of much of the detail already given under rhinitis and rhinosinusitis, but this is done in order to emphasize certain clinical implications.

As a substitute for the complicated classification offered under chronic rhinosinusitis the following could be used:

1. Acute congestive, analogous to acute evanescent rhinitis leaving no residuum.
2. Acute suppurative.
3. Chronic suppurative.
4. Chronic nonsuppurative, frequently allergic, with edema and hyperplasia.
5. Chronic mixed, due to infection and allergy.
6. Cystic and polypoid, the result of infection, allergy, or both.
7. Papillary.

Acute Congestive Sinusitis.—In the acute phase the capillaries are dilated, the stroma is swollen with serous exudate containing a few leukocytes, but the epithelium is intact. Later the exudate begins to escape through the surface epithelium and becomes mixed with mucus and bacteria. Hemorrhages usually occur if the infectious agents are the more virulent streptococci. Resolution may occur in this stage by absorption of the exudate and subsidence of the vascular reaction. On the other hand, the exudate may become more purulent and the inflammatory phenomena may persist, resulting in tissue damage that requires repair. The inflammatory reaction can involve the periosteum and extend into the bone, giving rise to osteomyelitis and other complications discussed in more detail in the section on intracranial complications. Eagleton has called attention to the tendency of the roof of the sphenoidal sinus to be perforated if the infecting organism is the pneumococcus.

Acute Suppurative Sinusitis.—In suppurative sinusitis a variable number, sometimes astonishingly few, polymorphonuclear cells appear just under the epithelium in the loose subepithelial connective tissue. As the infection subsides the purulent discharge becomes mucopurulent, of a greenish, brownish, or yellowish color; it then becomes grayish and less purulent, and finally clear. Histologically, in the healing stage the number of polymorphonuclear leukocytes in the mucous membrane decreases, but excessive numbers of well filled goblet cells persist for some time.

Chronic Suppurative Sinusitis.—The infectious nature of the process is evidenced histologically by the admixture of polymorphonuclear leukocytes with the ubiquitous lymphocytes and plasma cells, at times to the extent of abscess formation. This leads to serious complications if adequate drainage is not instituted. Ulceration of the mucosa and extensive necrosis may also be evident.

The gross appearance of the mucous membrane, as seen at the time of operation, varies considerably, depending upon the duration of the infection and the degree of ulceration and fibrosis. In typical empyema the membrane is usually 1 to 2.5 mm. in thickness, the surface is covered with pus and granulations (granulation tissue), and the entire membrane is red from congestion, bleeds freely, and is usually rather friable. It is loosely attached to the bony walls and, when necrosis is marked, is partly detached and even floating in the purulent contents of the cavity, exposing the bone. Much fibrosis, including thickening of the mucoperiosteum and new bone formation, is found in chronic cases of long standing. Additional clinical features are villous or polypoid thickenings of the mucosa, gross cysts or pseudocysts, and frank polyps presenting in the sinus cavities or protruding through the ostia. Polyps are seen most commonly in the ethmoidal and maxillary sinuses. Occlusion of the ostium by polyps results in empyema of the sinus.

Microscopically, the epithelium is reduced to one or two cell layers through the desquamation of the superficial ciliated cells, is entirely lost, or undergoes metaplasia to the squamous type. The basement membrane shows varying degrees of thickening and hyalinization in relation to the chronicity of the process and the extent to which allergy is concerned in the etiology. The mucous glands are atrophic or hyperactive. The stroma of the mucosa is lacy from serous exudate-edema, or thickened and dense from scar tissue. The amount and character of the exudate varies considerably depending on the stage of the reaction and on the etiologic factors involved. The specific changes which reflect an allergic factor in the etiology have been described. In the absence of allergy as a factor, the exudate is mononuclear, particularly rich in plasma cells, with a surprisingly low content of polymorphonuclear leukocytes. At times the exudate is concentrated around the blood vessels and glands, particularly when there is much interstitial edema. When this feature of activity is absent, the cells are more diffusely scattered through the stroma. When the condition is particularly chronic and of sluggish activity, secondary lymphatic follicles may develop as described in chronic rhinitis and become a prominent histologic feature.

With the subsidence of the active reaction, any granulation tissue that has developed undergoes the same regression that it does in other situations. There is diminution in the amount of cellular and serous exudate, and the connective tissue becomes less and less cellular from pressure of the accumulating collagen. With the contraction of the collagenous connective tissue there is a reduction of the vascular elements and sclerosis of those that remain. Finally the mucosa becomes simply scar tissue, with or without an epithelial covering.

Under ordinary circumstances re-epithelization of the respiratory mucosa is accomplished readily, but it is easy to understand what a poor chance there is for restoration of physiologically competent epithelium on the surface of avascular scar tissue. When there is empyema of the sinuses, the periosteum is more actively involved and osteoclastic and osteoplastic activity are evident.

Chronic Sinusitis. — To recapitulate, the term chronic sinusitis is used when excessive mucus, mucopus, or actual pus persists in the paranasal cavities, and roentgenograms reveal edematous and hyperplastic thickening or cystic and polypoid degenerative changes. The term hyperplastic sinusitis is used to indicate chronic sinusitis with minimal suppuration and moderate or marked mucosal thickening. These changes occur more frequently in the presence of an allergic constitution. The chronic edematous forms in which there is uneven thickening are often stages in the development of the hyperplastic form.

The pathologic changes in all types include alterations in the character of the epithelium, e.g., loss of cilia, desquamation, mucinous degeneration, hyperplasia, or metaplasia. The basement membrane may show hyalinization and thickening. The tunica propria becomes edematous and displays a cellular infiltrate composed of lymphocytes and plasma cells. The presence of polymorphonuclear cells, histiocytes, and fibroblasts varies with the different types of sinusitis. Thickening and fibrosis in the walls of the vessels may lead to their obliteration. Granulation tissue appears only as a result of suppuration and ulceration. The periosteum thickens and becomes more fibrous in low-grade purulent infections, with consequent bone proliferation. The nonsuppurative, edematous, and polypoid forms may lead to thinning of the bone, apparently from pressure rather than from infection and osteoclastic action.

Cellular Exudate in the Sinuses.—Polymorphonuclear neutrophils are less conspicuous in sinusitis than one would expect, and for this reason close scrutiny of the infiltrate is necessary to determine the presence or absence of pyogenic infection. As a rule, all that can be seen in a case of chronic purulent sinusitis is an infiltration consisting of histiocytes, plasma cells, and lymphocytes; however, the presence of scattered polymorphonuclear neutrophils, especially in the vicinity of the epithelium, is sufficient to warrant a diagnosis of pyogenic sinusitis. The typical focal collections of suppurative inflammation are rarely seen in surgical specimens and then only when ulceration and necrosis are imminent or actually present.

A variable number of lymphocytes, plasma cells, and a rather high proportion of histiocytes appear in all forms of sinusitis. As a rule the infiltrations are more dense in the subepithelial region but may be scattered throughout the entire thickness of the loose layer of connective tissue. The exudate may invade the periosteal layer, but this suggests extension of the infection to the bone. Much more common in ordinary surgical material are areas of halisteresis and of osteoid growth, with no purulent exudate in the immediate neighborhood.

Eosinophils, when present in subacute and chronic sinusitis, may be due to infection only, but large numbers of such cells should arouse suspicion of an allergic factor. Where allergy and suppuration are combined, which is the most common picture of all, the ubiquitous round cells continue to dominate, but here and there eosinophilic and pyogenic exudation can be detected. In such cases the diagnosis of purulent sinusitis can be made on the basis of polymorphonuclear exudation, but the allergic process can be recognized only by considering the picture as a whole, including the clinical history and such microscopic evidence as hyalinization of the basement membrane of the mucosa.

Chronic Polypoid and Cystic Sinusitis.—In advanced cases of allergic sinusitis the whole sinus cavity may be filled with edematous polyps hanging from the walls in swollen masses. Actual suppuration is seldom seen, but much mucoid exudate is commonly present. The connective tissue spaces rupture and form large cystic cavities filled with serum, and the few mucous glands that are present dilate and become cystic. Thus two types of cysts arise, (1) pseudoserous and (2) mucus retention. The serous cysts contain amber-colored fluid and the retention cysts contain thickened grayish mucus; secondary infection may produce abscesses in either.

Histologically, the polypoid specimens present an edematous stroma with hyperplastic changes and numerous cysts. In most instances the swollen degenerated mucosa forms sessile polyps or pedunculated ones that extend through the sinus ostia and hang in the nasal cavity. The sessile polyps may undergo spontaneous resolution and disappear, but the pedunculated polyps are less likely to disappear spontaneously. Bilateral polypoid pansinusitis is usually the result of allergy. Allergic polyposis recurs, but not as frequently when desensitization treatment is used. Polyps *per se* are discussed in the next chapter.

Bony changes in chronic sinusitis are of two types: (1) destructive, (a) by osteoclastic resorption and (b) by halisteresis, a bland resorption of bone without the aid of osteoclasts; or (2) osteogenic, the result of proliferation of the osteoblasts of the periosteal layer of the mucosa. Osteogenic activity may lead to eburnation of the bone, sometimes seen in the mastoid. No correlation can be made between change in the bone and that in the soft tissues, although polypoid and papillary sinusitis are frequently accompanied by osteolytic changes, and fibrotic sinusitis by osteoblastic changes.

SPECIAL ASPECTS OF SINUSITIS

The ethmoidal sinus is probably involved to some extent in every case of acute rhinitis, and chronic ethmoiditis is an important factor in the recurring type of rhinitis. In infants and young children it is the usual form of sinusitis, since the other sinuses, with the possible exception of the maxillary, are usually not sufficiently developed to be involved, and ethmoidal sinusitis is frequently a complication of the acute childhood diseases.

Because of the comparative thinness of the mucosa, infections are more likely to involve the bony lamella than in other sinuses. This leads to such complications as external fistulae, orbital cellulitis, inflammation of the lacrimal duct, intracranial infections and optic neuritis. Polyposis is a frequent complication of chronic ethmoidal sinusitis in adults, but it is seldom seen in children. In acute ethmoiditis the mucosa is congested and edematous, and there is drainage from the middle or superior meatus without evidence of infection in the frontal, maxillary or sphenoidal sinuses. The term "ethmoiditis" is used rather loosely and frequently denotes inflammation of the ethmoidal region of the nasal cavity, which may be either persistent rhinitis or may include actual involvement of the ethmoidal cells.

The Sphenoidal Sinus. – Acute sinusitis results from an infection of the nose or nasopharynx or as a complication of one of the acute examthems. It too may be overlooked, for although occipital headache is a characteristic symptom, it is not a constant one, and the headache can, of course, result from other lesions. Postnasal discharge is a common clinical symptom as are ocular manifestations, and meningitis may be a complication. X-ray examination is an important diagnostic procedure and exposures from several positions may be necessary to determine whether the sphenoid is involved.

Sinusitis in Children.–An important factor modifying the disease in childhood is the chronologic order of development of the various sinuses to the point where they become subject to inflammation. The ethmoidal sinus is well developed at birth, the sphenoidal and frontal sinuses are not fully developed until about the age of 12, and the maxillary sinus assumes adult form at puberty. The frontal sinus is the last to appear; it often fails to develop and is the least commonly involved of any of the sinuses in children.

Other influential factors in determining the incidence of sinusitis in children have been mentioned and include the relative abundance of lymphatic tissue in the fauces and the nasopharynx, the higher incidence of allergic reactions, and the incidental involvement of the sinuses in the common childhood diseases. It is not surprising, therefore, that rhinosinusitis reaches peak incidence in the group between 4 and 10 years of age.

Remote complications are more common in children than in adults. These include pyelitis, cervical adenitis, gastrointestinal disturbances, meningitis, brain abscess, and orbital cellulitis.

The basic pathologic features are the same as those of rhinosinusitis in adults, but they are usually less severe in intensity and less widespread in distribution. General hypertrophy of the nasal mucosa is accompanied by turgescence. The inferior turbinates are greatly enlarged, causing obstruction of one or both nares by impingement on the nasal septum. Bacterial infection is indicated by mucopus that bathes the turbinates. The source of this exudate can usually be traced to the maxillary sinus. Polyps are seldom seen, although allergic sinusitis usually produces polypoid changes in the mucosa.

Microscopically, the exudate shows the same modifications as in adult sinusitis, depending on the extent to which allergy and bacterial infection are factors. Frank ulceration is less common in children. The bone changes vary considerably. Atrophy due largely to pressure by the polypoid mucosa is seen particularly in the delicate ethmoidal septa and in the middle turbinate. Bone necrosis is not common.

Fulminant sinus disease in children has been studied by Lederer in an effort to determine the pathogenesis of acute osteomyelitis of the maxilla which is relatively common, especially in infants. The determination of the pathogenesis in individual cases is difficult, because by the time the patient comes under observation the picture is complicated by the spread of the infection, usually to cranial structures.

It is the general experience that orbital infection is the commonest clinical evidence of infectious sinusitis in children. It is manifested by the swelling of the lids, proptosis, and possible corneal ulcers. In older children involvement of the upper lid alone is characteristic of frontal sinusitis, and of the lower lid alone, of ethmoiditis. Orbital involvement is so often a complication of sinusitis that Theisen considers further confirmation of the diagnosis unnecessary when it is present.

In addition to purulent rhinitis and maxillary sinusitis as causes of maxillary osteomyelitis, there is the possibility of spread to the bone as a result of trauma to the maxilla during birth, from infections about the tooth buds, and occasionally as a result of thrombophlebitis secondary to severe infections of the buccal tissues.

Ethmoidal sinusitis is the most frequent complication of purulent rhinitis in children. The infection spreads in well recognized fashion directly through the ethmoidal walls as a result of osteomyelitis. Lederer concludes that infection may invade the cranium through congenital defects in the ethmomaxillary suture, in the bony wall of the lamina papyracea, or in the orbital wall of the maxilla. He regards thrombophlebitis of the communicating veins as the commonest means of transmission since there is no anatomic basis for the assumption that the infection is transmitted intracranially by the lymphatics.

Aerosinusitis.—Acute inflammation and hemorrhages of the sinus may result from rapid barometric changes, especially in flying at high altitudes, and particularly when the ostia are compromised by inflammation. The frontal sinus is the most commonly affected. Negative pressure may draw the infectious material into the sinuses. Campbell reports that aerosinusitis results from a pressure differential between the inside and the outside of the sinus following an environmental pressure change, more often during descent. Complications are mucoceles and more commonly hematomas consisting of an accumulation of blood and fibrin in the loose tissues between the periosteum and mucosa. Such a lesion may resolve in a few weeks to a few months. Recovery from the acute symptoms of aerosinusitis usually follows equalization of pressure. A clinical characteristic is the stinging pain during ascent or descent, and a bloody mucoid discharge in the middle meatus is not uncommon.

Flying aggravates any existing sinusitis, and oxygen does little to minimize this effect. Removal of obvious anatomic impingements may help.

Aerosinusitis usually occurs in persons with large sinuses. It has been mistaken for a precancerous or an actual malignant condition. Metaplasia of epithelium to squamous type is a characteristic feature.

Does Sinusitis Ever Heal Completely?—It is possible even after long-standing fibrosing reactions for the epithelium to become comparatively normal and the patient free of symptoms. It is more likely to be true in the nonallergic cases in which the infection can be controlled before the mucosa is damaged to the extent that results in its replacement by scar tissue of low vitality. The repeated and almost constant insults of allergy cause extensive loss or alteration in the epithelium, the development of a thick basement membrane, and fibrosis of the stroma. The resulting lining of the sinus is usually not physiologically competent.

Surgical denudation results in replacement by a postoperative membrane consisting of scar tissue that usually becomes completely epithelized, but again is a poor substitute for the normal mucoperiosteum.

Suzuki outlines the stages of repair of the sinus mucosa after radical surgical removal as follows:

1. Granulation tissue dominant up to 10 days.
2. Sinus wall well covered with granulation tissue in 20 days.
3. New epithelium of squamous or cuboidal type well developed in 30 days.
4. Return of epithelium largely to ciliated, pseudostratified type in 50 days. Replacement of subepithelial tissue by scar.

Chronic purulent sinusitis that fails to respond to conservative methods of drainage may be the result of infection of deep-seated mucous glands. Nonpurulent hyperplastic sinusitis rarely requires surgical intervention. Most of these cases are allergic, especially when bilateral. The basis of treatment in these is correction of the allergic state.

COMPLICATIONS OF SINUS DISEASE

Retrobulbar neuritis is not as common a complication of sinusitis as it apparently was in former years. It is possible, however, for an inflammatory reaction in the ethmoidal or sphenoidal sinuses to extend to the sheath of the optic nerve. A more common experience is the development of edema of the optic nerve in allergic sinusitis. The possibility of confusing optic neuritis associated with minimal sinusitis with multiple sclerosis must be borne in mind.

Orbital cellulitis or **abscess** as a complication of frontal sinusitis is more frequent in adults, and similar lesions resulting from the ethmoidal or maxillary infection more frequent in children. Usual contributing features are congenital dehiscences along the ethmomaxillary suture and the lamina papyracea or the orbital wall of the maxilla, though the infection may reach the orbit through the intracranial blood sinuses by retrograde thrombophlebitis without bone involvement. An infection of the ethmoidal sinus may not involve the orbit but may point through the inner portion of the upper lid. From infections of the maxillary sinus the pointing is through the lower lid. Orbital cellulitis in children has been described in a preceding section of this chapter.

Osteomyelitis of the Frontal Bone.—In children it is always a hematogenous infection; in adults, however, it usually results from the spread of infection in the frontal sinus. Most patients are under

30 years of age. Trauma, swimming, or operative procedures frequently precede the osteomyelitis, which may extend into other bones by thrombophlebitis of the diploic veins. It may extend, also, by direct penetration of the wall of the sinus, either beneath the meninges to form an intracranial abscess, or beneath the external periosteum to produce a subcutaneous abscess. The thrombophlebitis usually extends for a much greater distance than is clinically evident, and before the availability of antibiotics very wide removal of the frontal bone was necessary in order to eliminate the infection.

Osteomyelitis of the Maxillary Bone.—One of the less common causes is the extension of an infection from the maxillary sinus. Once established, further extensions are possible: (1) to the skin surface, forming troublesome fistulae; (2) to the roof of the mouth, a serious matter in children because tooth buds can be destroyed; (3) to the zygomatic process with necrosis of the arch, from which it may reach the pterygoid fossa and result in an abscess. The subject is also discussed in the section on sinusitis in children.

Osteomyelitis of the ethmoid extends by thrombophlebitis to the cavernous sinus, or by erosion through the ethmoidal wall to the periorbital tissues, resulting in abscesses.

Osteomyelitis of the sphenoid is rare. It may result from the extension of an infection of the petrous portion of the temporal bone and be complicated by meningitis, brain abscess, or thrombosis of the cavernous sinus.

Osteomyelitis of the skull is a progressive infection of the marrow with necrosis of the entire thickness of the bone. It is a complication of frontal sinusitis or, in infants, may begin as ethmoiditis. It arises in the maxilla following dental extractions, and invades the middle fossa of the skull. It may follow fractures or operations on the frontal sinus. Bacteria invade the canaliculi and medullary spaces of the bone and spread through these channels. There is septic thrombosis of the veins of Breschet and communicating venous channels which interrupts the circulation and creates isolated islands of osteomyelitis in advance of the main focus of involvement.

Early in the course of the disease there are no visible changes in x-rays or gross specimens; later there is hyperemia of the diploe, and in about ten days the bone softens and the medullary spaces exude much pus, show granulations and thrombosed vessels. The color of the bone changes to red or black, and abscesses lift the periosteum and dura mater from the bone, severing the periosteal blood supply and giving rise to "puffy tumors" in the scalp. Sequestration, or isolation of the dead portions of the bone, finally occurs, largely as a result of the lack of circulation.

Mucocele of Sinuses.—Mucocele is either an accumulation of mucoid secretion in a sinus, usually from blocking of its ostium, a retention cyst of a mucous gland, or cystic degeneration of a polyp. The bony walls of the sinus may become thin from pressure atrophy or actual erosion. The sphenoidal and maxillary sinuses are rarely involved; most commonly affected are the ethmoidal and frontal sinuses in late middle life.

There is pressure atrophy of the epithelium and the mucosa is thin. In the late stages there may be fibrosis of the cyst wall.

Pyocele of sinus results from infection of a mucocele.

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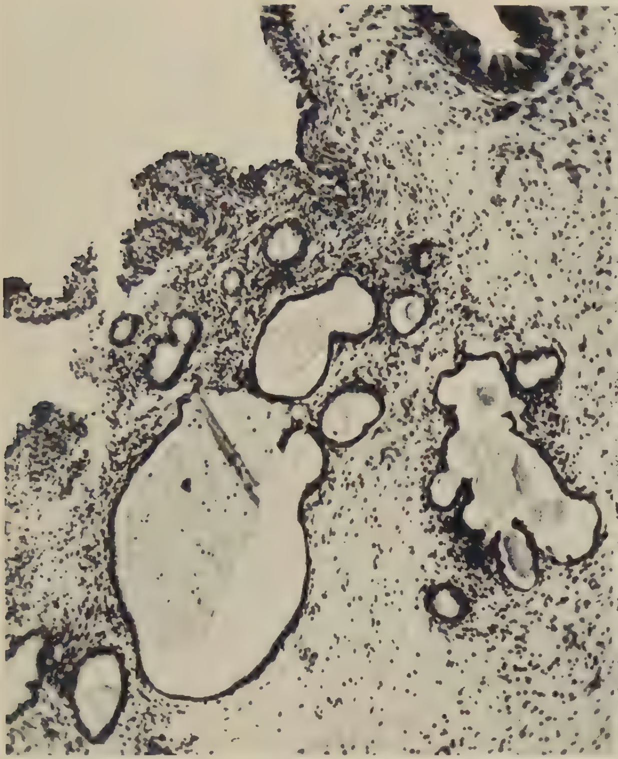
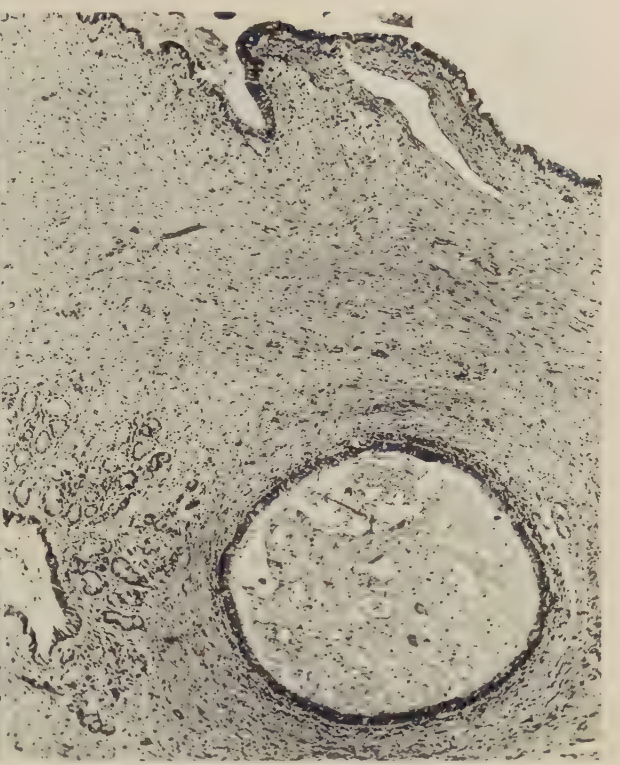
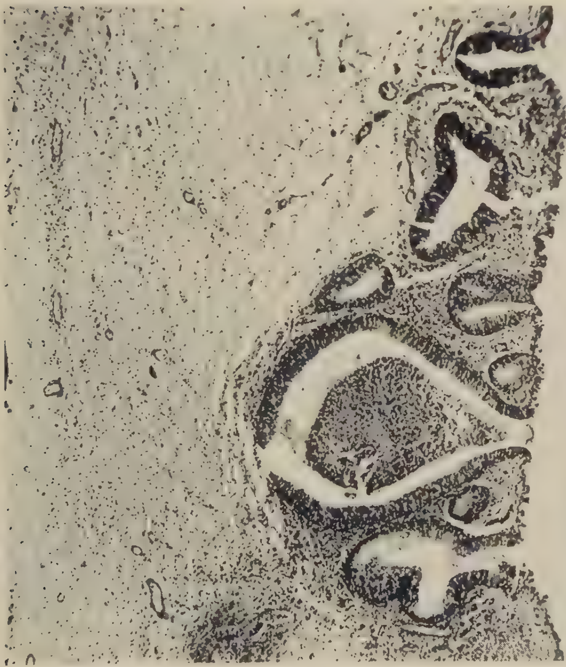
PATHOGENESIS OF TRUE CYSTS



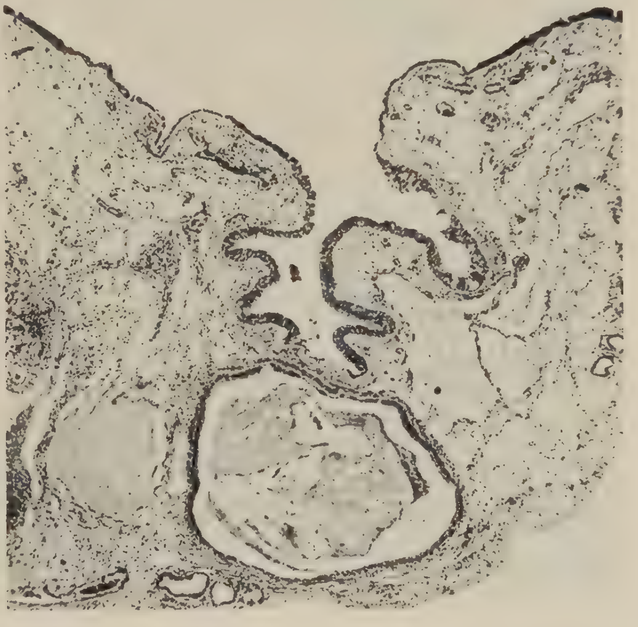
Obstruction of ducts of seromucinous glands near surface, with retained secretion and dilation which extends into acini. Chronic maxillary sinusitis.



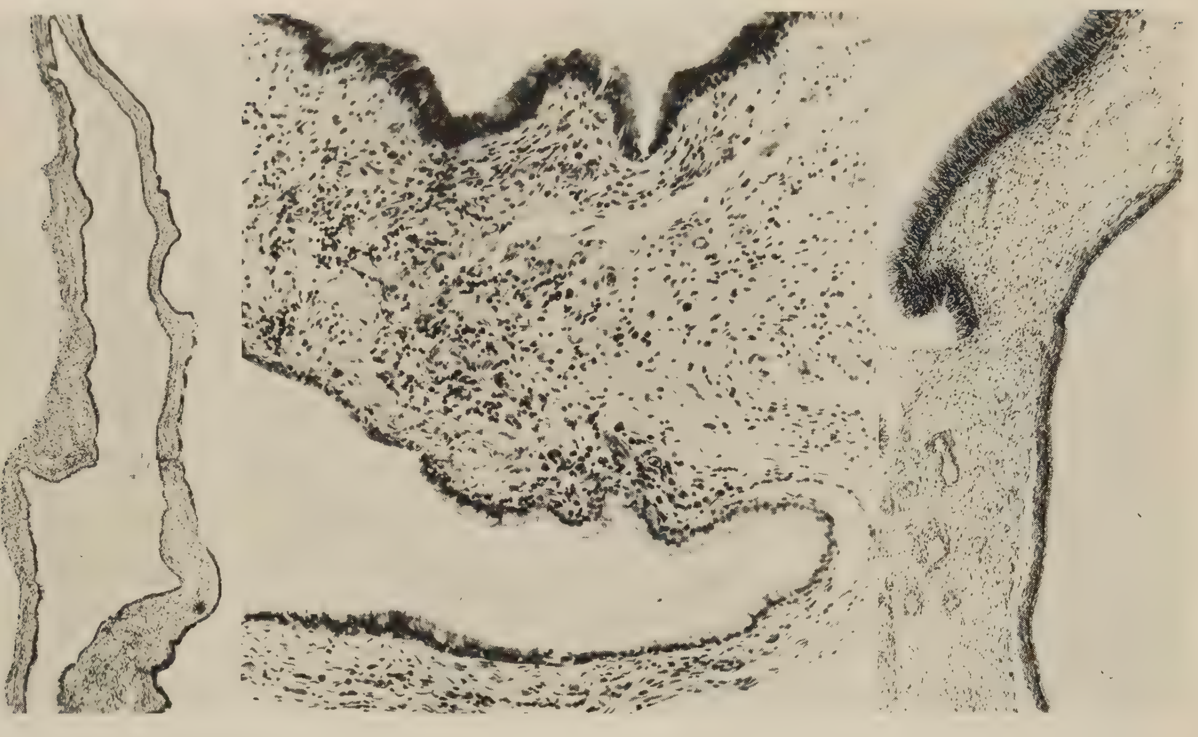
Epithelial inclusion or an occluded duct may have caused this cyst, the ciliated epithelium of which is identical with that of surface epithelium and adjacent gland duct. Fibrotic ethmoid sinusitis. x 48.



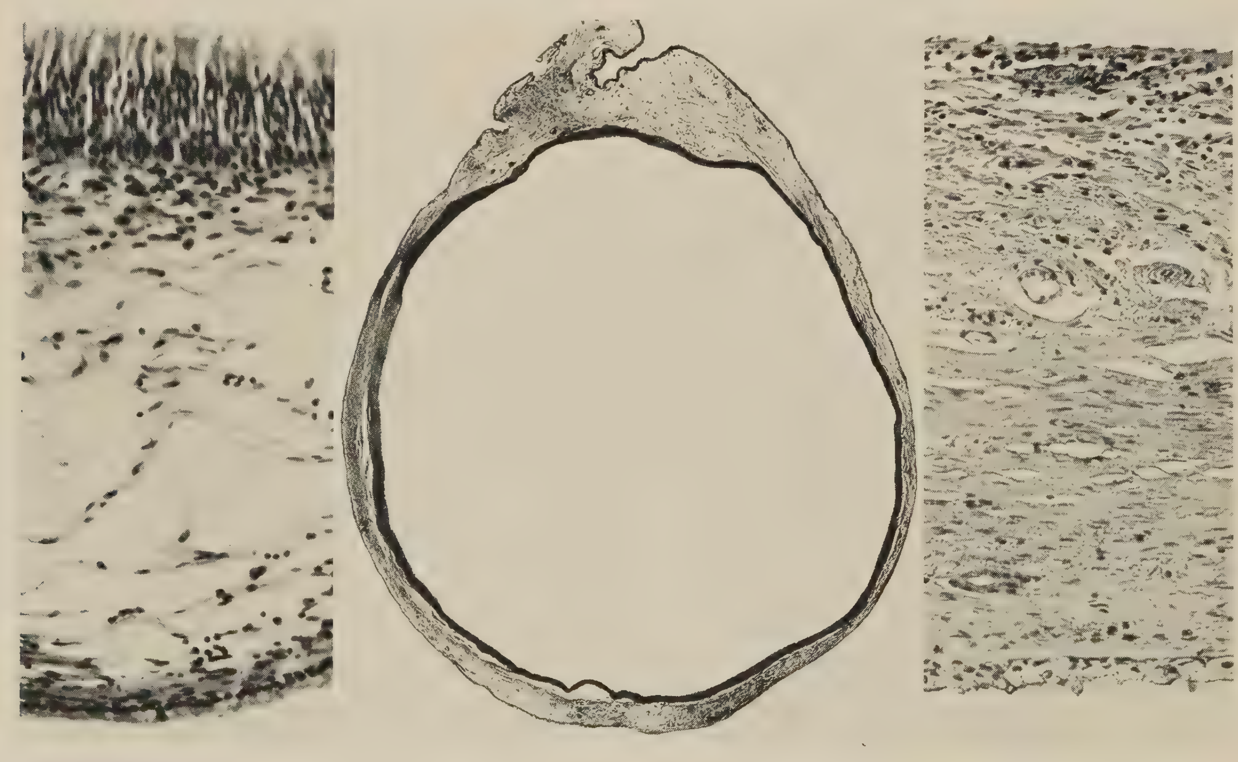
Downgrowths of surface epithelium form "pseudoglands" that are dilated because of narrowed orifices. Complete occlusion may be the result of continued inflammation and subsequent fibrosis. Chronic maxillary sinusitis. x 48.



Retention cyst or epithelial inclusion cyst in chronic maxillary sinusitis, lower center. Deeply infolded surface epithelium with approximation of apposed polypoid surfaces, parts of which may fuse. Interstitial pseudocyst at left. x 48.

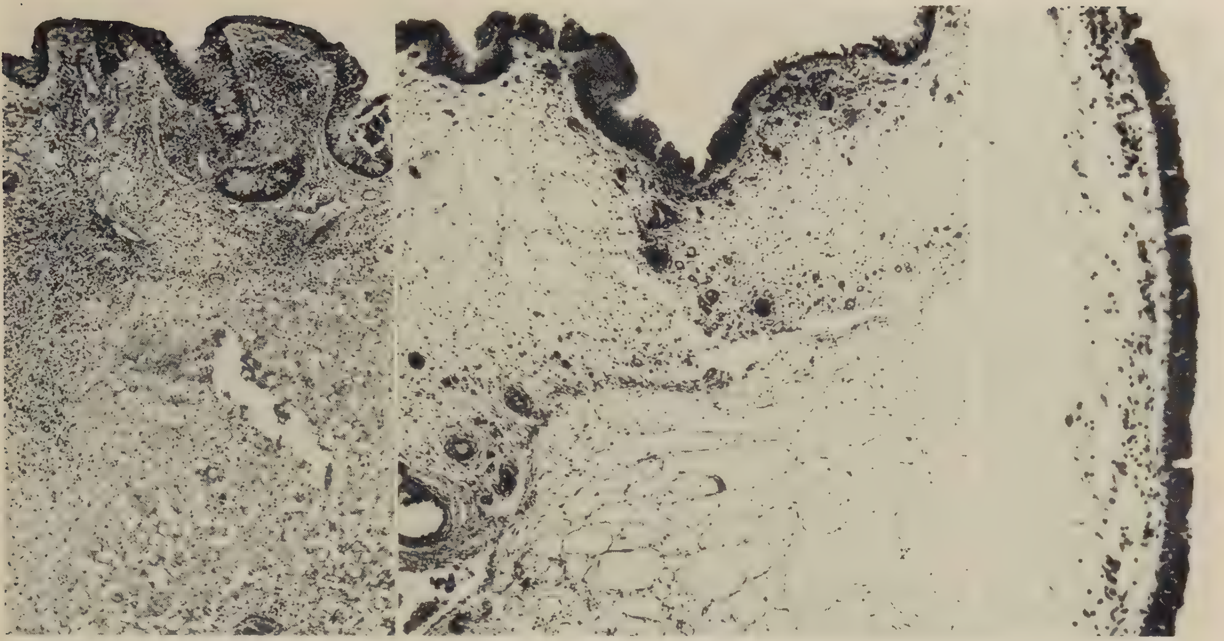


A. Large collapsed mucous cyst, maxillary sinus mucosa (sinus epithelium to right). x 48. **B.** Magnified field shows relatively normal sinus mucosa at top. Lining of cyst varies from tall columnar, ciliated, mucus-producing epithelium to cuboidal and flattened cells. Fibrosis and chronic exudate in intervening stroma. x 125. **C. Segment of dilated mucous cyst** in maxillary sinus mucosa, at right. Surface epithelium of sinus, upper left. x 55.

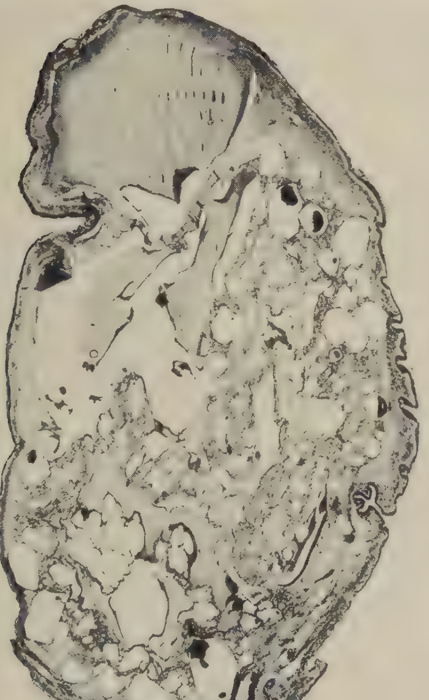


D. Magnified field of **C.** Normal sinus epithelium at top. Cyst lining composed of a single row of cuboidal cells, around which adjacent compressed fibrous tissue strands form a thin fibrous wall. x 185. **E. Cyst, probably retention type,** but possibly part of a true mucocele (dilation of sinus cavity itself with accumulation of secretion) involving portion of ethmoid labyrinth. Mucosa covers entire circumference (x 10) and in **F.** shows epithelial desquamation to flattened basal layer (at top). At bottom, cuboidal and flattened epithelium of cyst with thick fibrous wall. x 150.

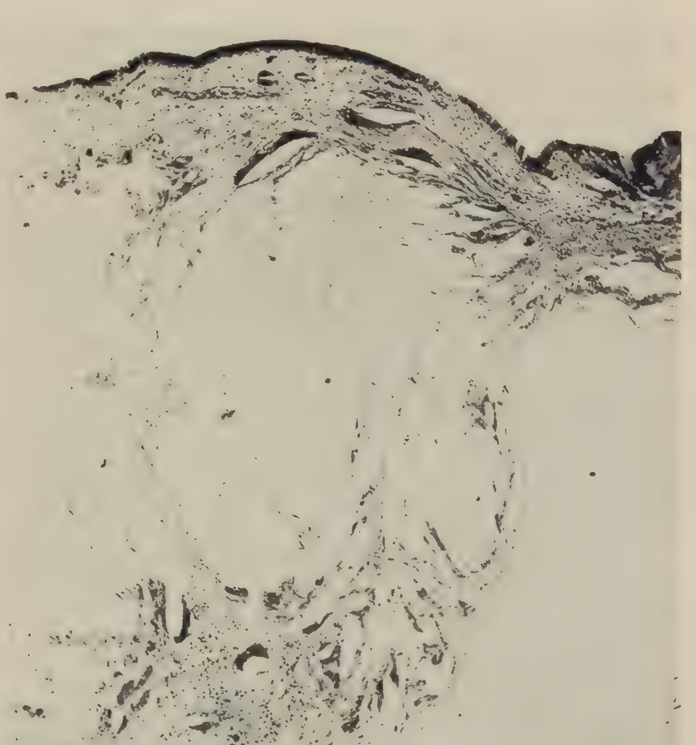
PATHOGENESIS OF PSEUDOCYSTS ("INTERSTITIAL CYSTS")



Development of the "interstitial cyst" or pseudocyst. A. Very edematous tunica propria. x 48. **B.** Some connective tissue septa have ruptured, others are stretched to form larger spaces, some containing edema fluid. x 48. **C.** A large space without epithelial lining. Surface epithelium at right. x 125.

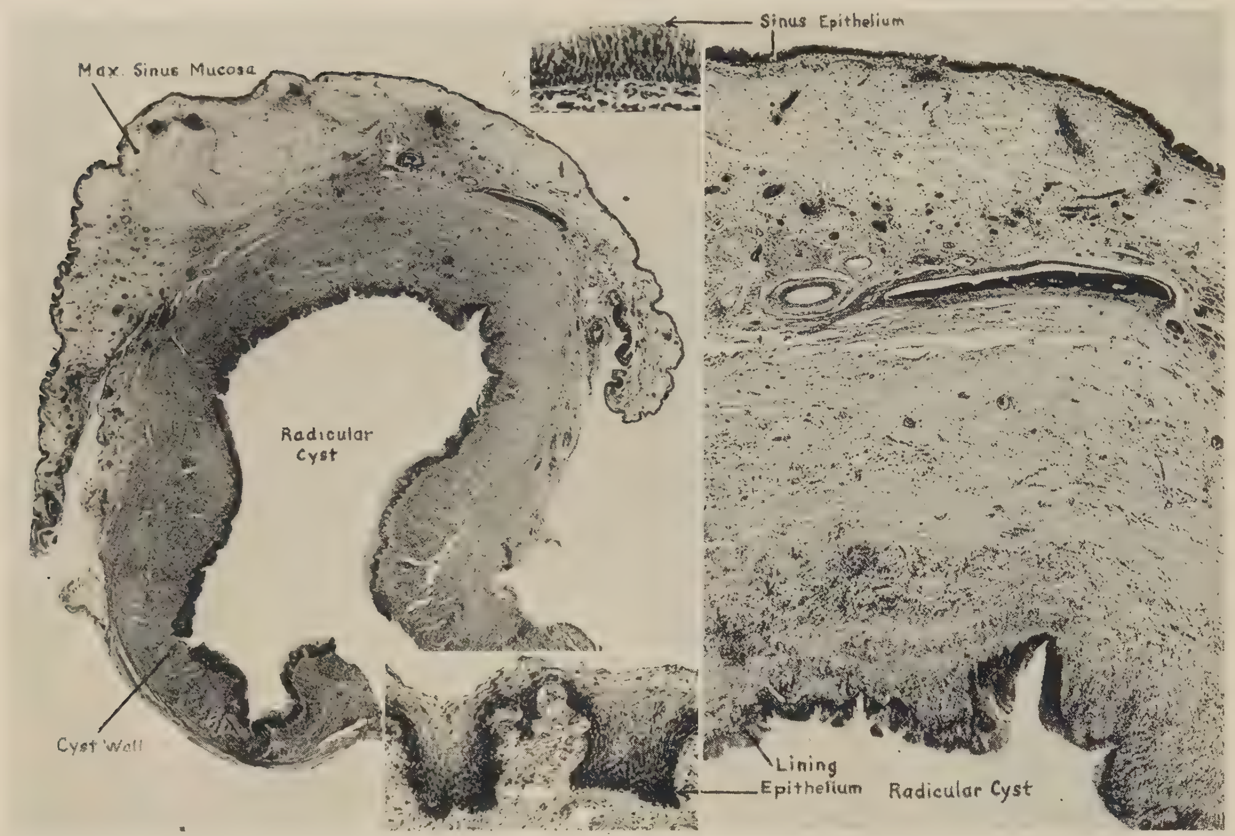


Pseudocysts, some containing coagulated protein fluid, honeycomb stroma. Case of hyperplastic sinusitis in which x-rays suggested malignancy. x 8. (S. S. Hall, Clarksburg, W. Va.)

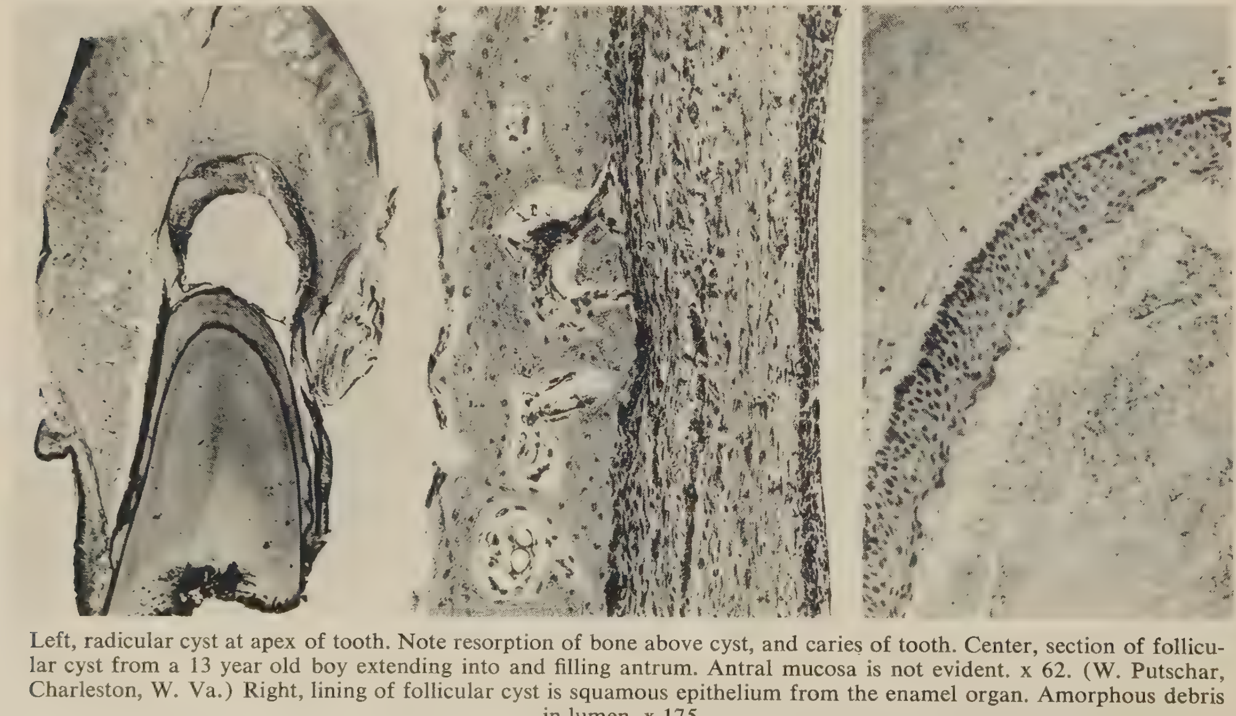


"Rhinitis caseosa pseudo-cholesteatoma," of varied etiology, may show interstitial pseudocystic structure, as above, with cholesterol clefts and foreign body giant cells. x 48.

RADICULAR AND FOLLICULAR CYSTS INVADING MAXILLARY SINUS

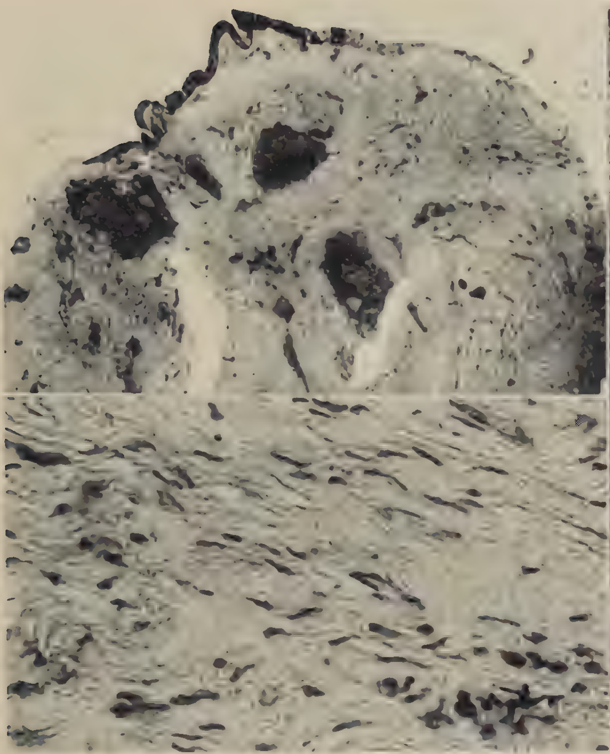

Sinus Epithelium
Max. Sinus Mucosa
Radicular Cyst
Cyst Wall
Lining Epithelium
Radicular Cyst

Radicular cyst on a molar tooth (x 9) has eroded into antrum, pushing the antral mucosa ahead of it (at top). The cyst wall is dense fibrous tissue lined by squamous epithelium (lower inset, x 75). The antral mucosa is edematous and congested and its epithelium has retained its respiratory character (upper inset, x 125). Right, between the two membranes is a spicule of bone from the floor of the antrum. x 24.

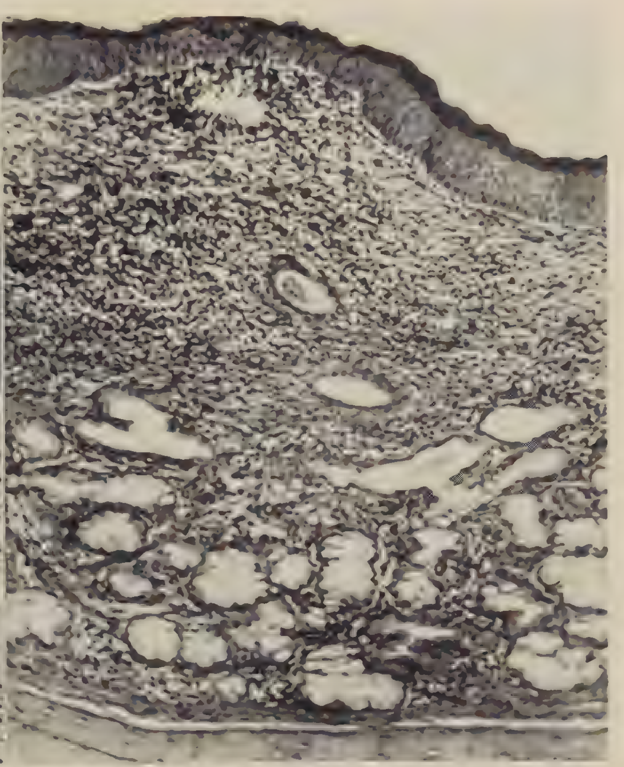


Left, radicular cyst at apex of tooth. Note resorption of bone above cyst, and caries of tooth. Center, section of follicular cyst from a 13 year old boy extending into and filling antrum. Antral mucosa is not evident. x 62. (W. Putschar, Charleston, W. Va.) Right, lining of follicular cyst is squamous epithelium from the enamel organ. Amorphous debris in lumen. x 175.

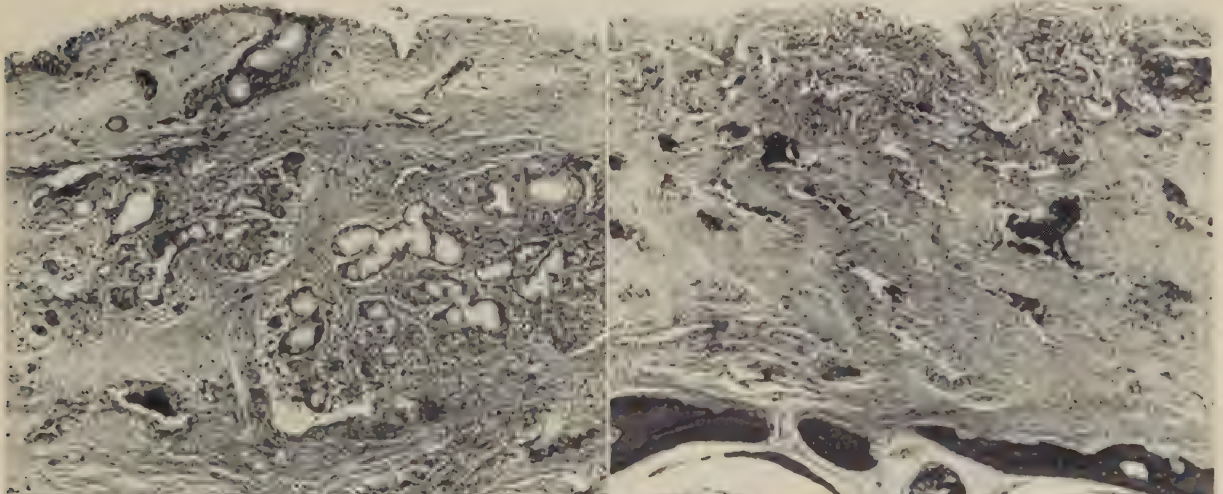
SCLEROSING RHINOSINUSITIS



Postoperative fibrosis, maxillary sinus. **A.** Concentrations of round cells in scar tissue. **B.** Dense scar tissue removed 8 years after first Caldwell-Luc operation. (Semenov).

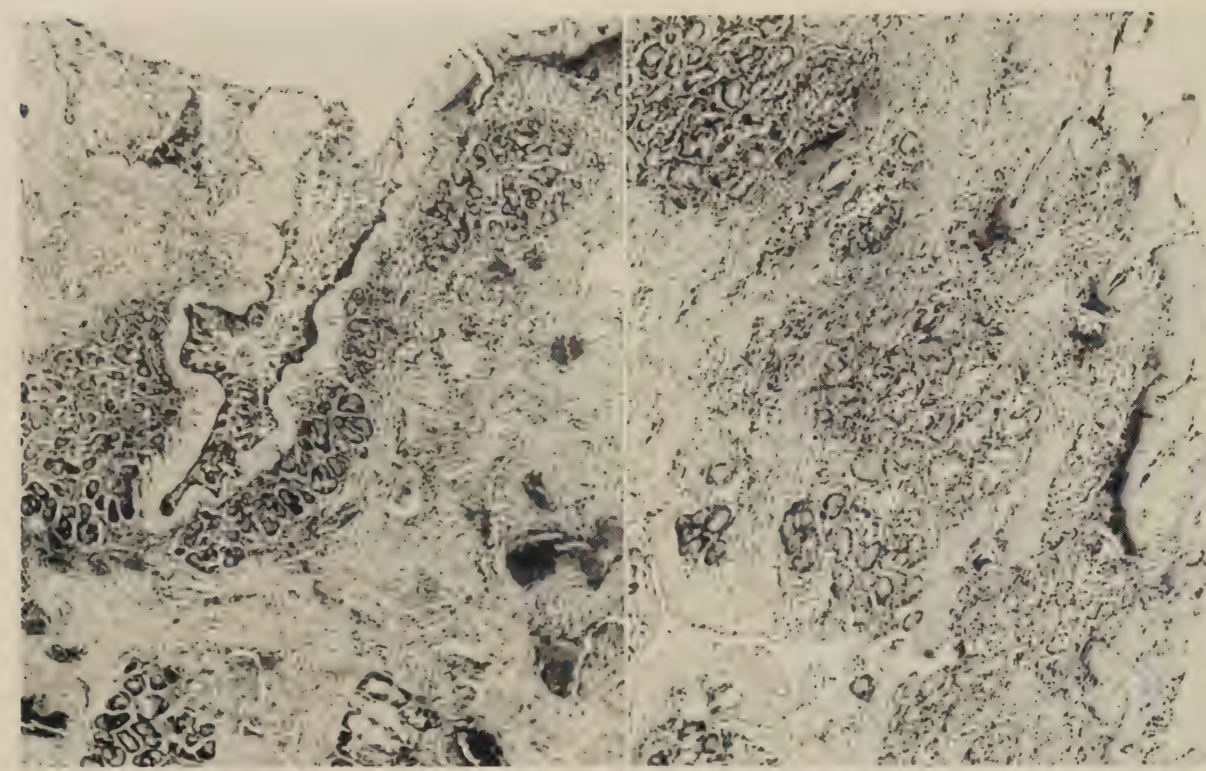


Chronic sinusitis with fibrosis and squamous metaplasia of surface epithelium. Very evident secretory activity and dilation of glandular acini indicate probable early obstruction of the glandular duct. (Semenov).

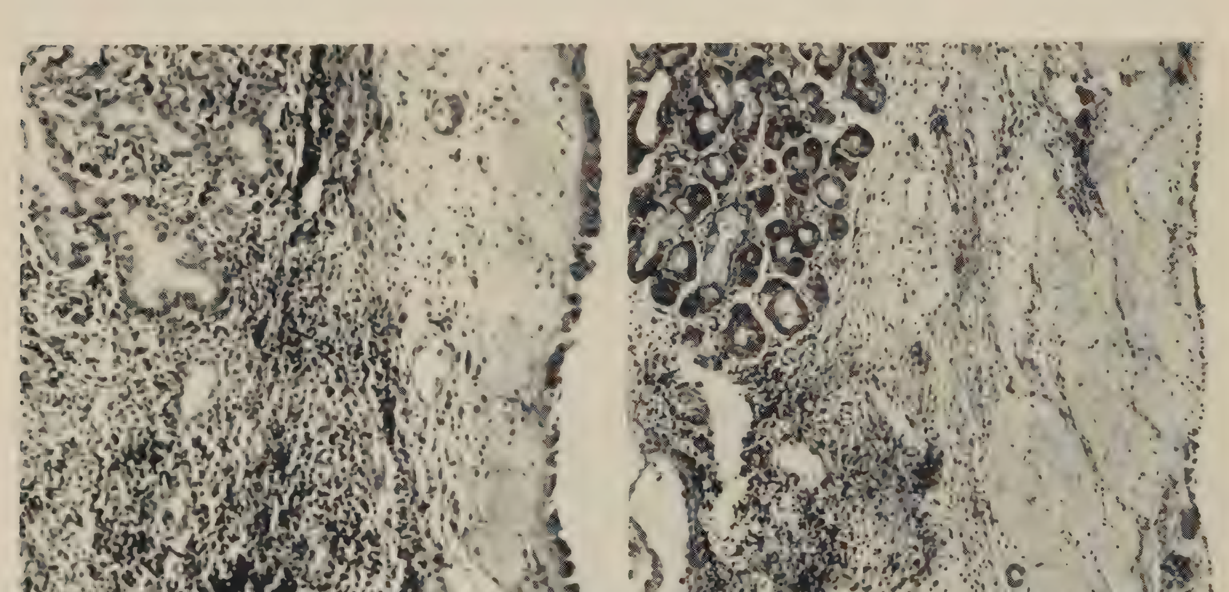


Chronic rhinitis ("atrophic," fibrotic, sclerotic). Clinically these membranes may be thicker than normal, as specimens above from right and left turbinates of same patient. Epithelium partially desquamated and altered, stroma densely fibrous; glands atrophic. At right, congested and thick-walled cavernous plexus in more vascular area. Turbinal bone and dilated vessels at bottom. Both x 48.

PATHOLOGIC BASEMENT MEMBRANE



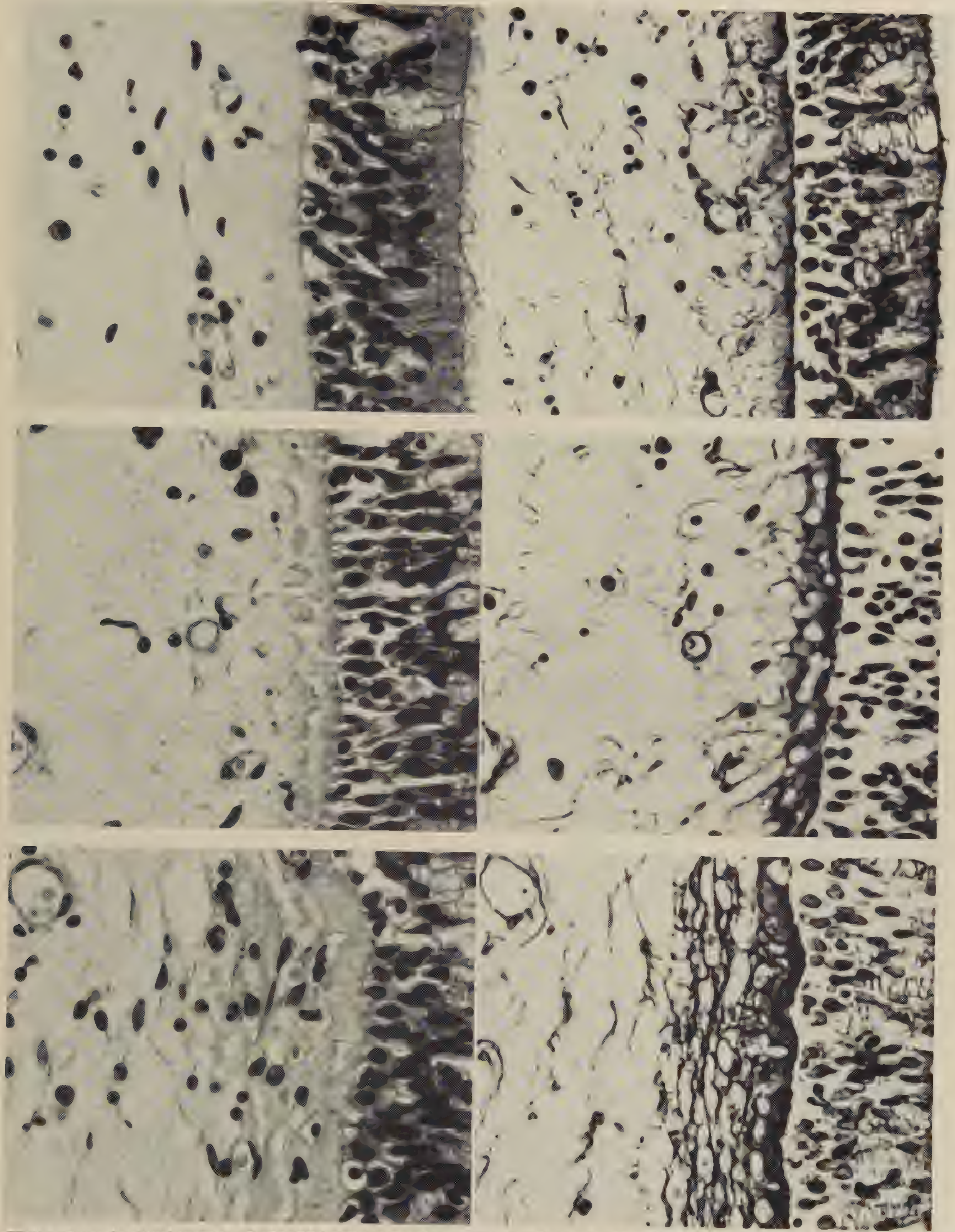
Hyalinized, thickened membrana propria, turbinal mucosa, including that of gland duct, from a 53 year old man with history of rhinosinusitis and recent recurrent epistaxis. Surface epithelium represented by only a few basal cells; stroma densely fibrosed; glands atrophic. x 48, x 76.



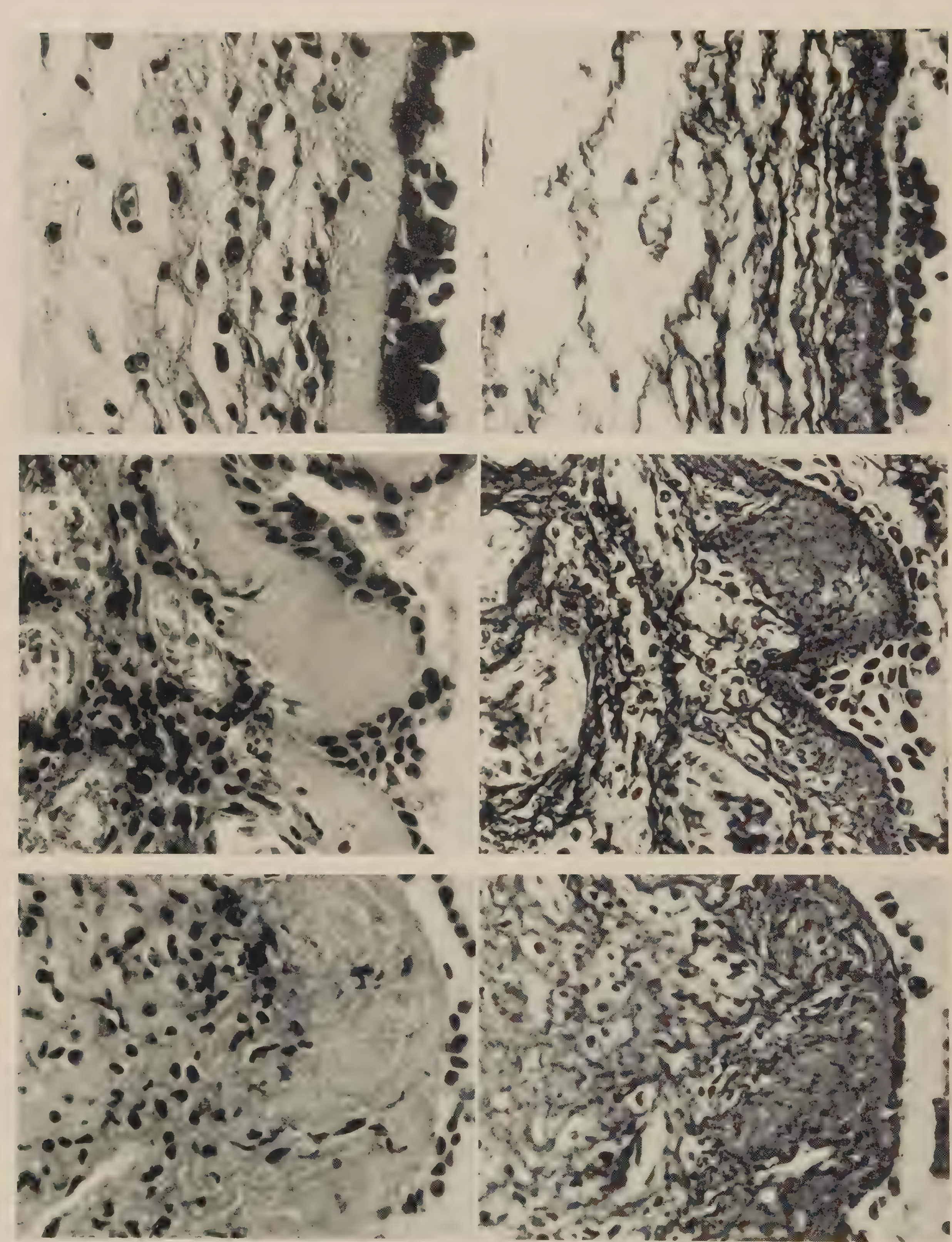
Extreme thickening of basement membrane of turbinate (x 145), which appear convoluted at right (x 100), from another case of bilateral rhinosinusitis, probably of allergic etiology with superimposed infection. Dense chronic inflammatory exudate; marked fibrosis; atrophy of glands.

CHRONIC RHINITIS

I. DEVELOPMENT OF PATHOLOGIC BASEMENT MEMBRANE

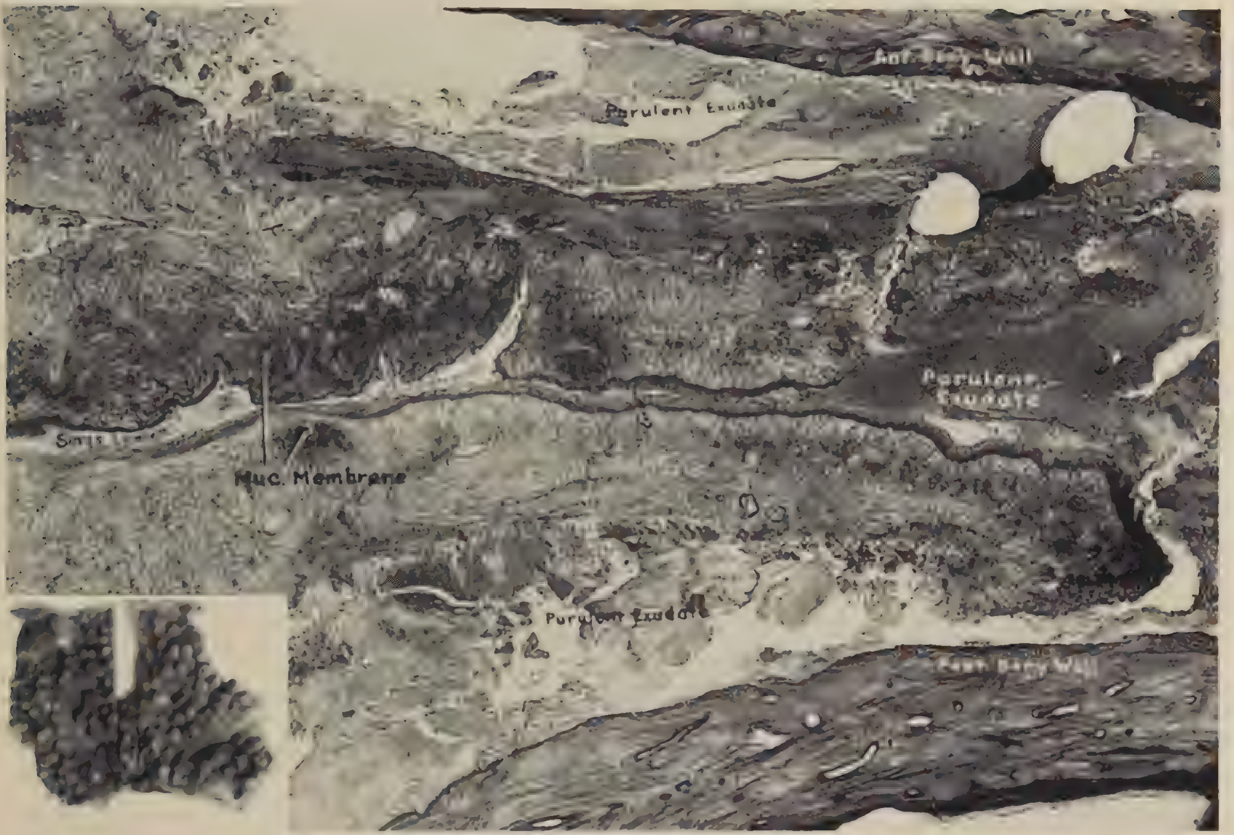


Three stages in development of the thick hyalinized basement membrane in chronic "allergic" rhinosinusitis; in left column, hematoxylin and eosin-stained sections; in right, silver impregnations to demonstrate reticulum fibers. Reticulum cells are still evident in the accumulating reticulin. All x 500.

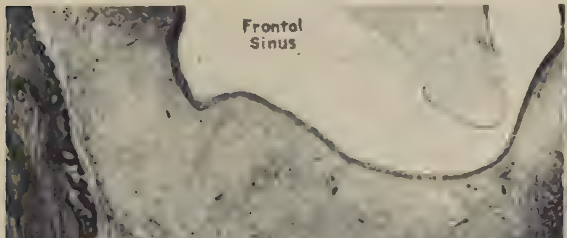


Later stages in the development of the thick basement membrane. Hematoxylin and eosin-stained sections in left hand column, silver impregnated ones in right. As the reticulin accumulates and condenses, the membrane becomes thicker and more hyalinized and the reticulum cells reduced. Case of "allergic" rhinosinusitis with superimposed infection. All x 500.

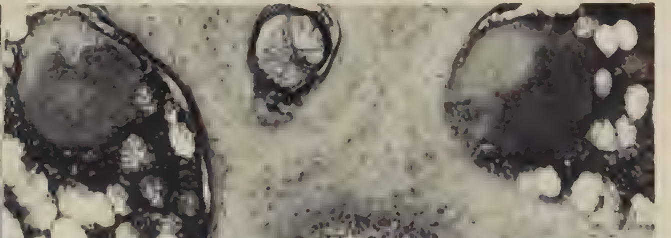
PATHOGENESIS OF COMPLICATIONS


Ant. Bony Wall
Purulent Exudate
Purulent Exudate
Sinus
Muc. Membrane
Purulent Exudate
Post. Bony Wall

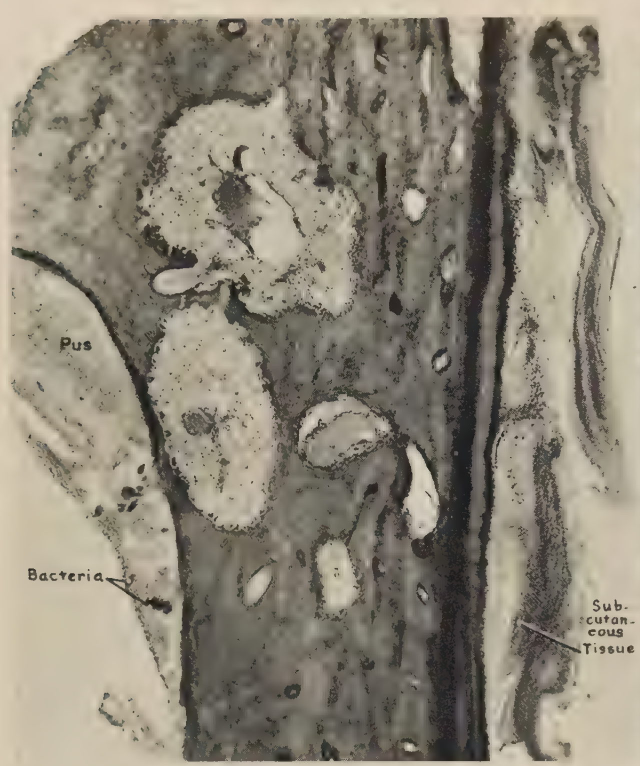
Suppurative frontal sinusitis. Pus fills cavity of sinus at right, and is also undermining acutely inflamed thickened mucosa over anterior and posterior bony walls. x 28. (H. P. Mosher, Boston). Inset: Gross appearance of mucosa in purulent frontal sinusitis. (Semenov).


Frontal Sinus

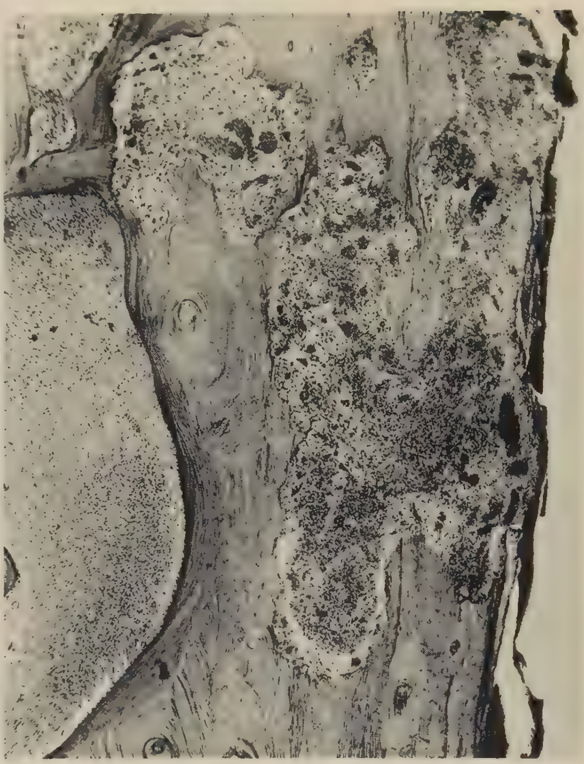
Exudate—and infection—find direct access from sinus to (a) haversian systems of surrounding compact bone through ostia (arrows) for vessels to the mucosa (above x 21); or to (b) cancellous diploic bone and its venous systems producing **septic thrombophlebitis** and **osteitis** or **osteomyelitis.**



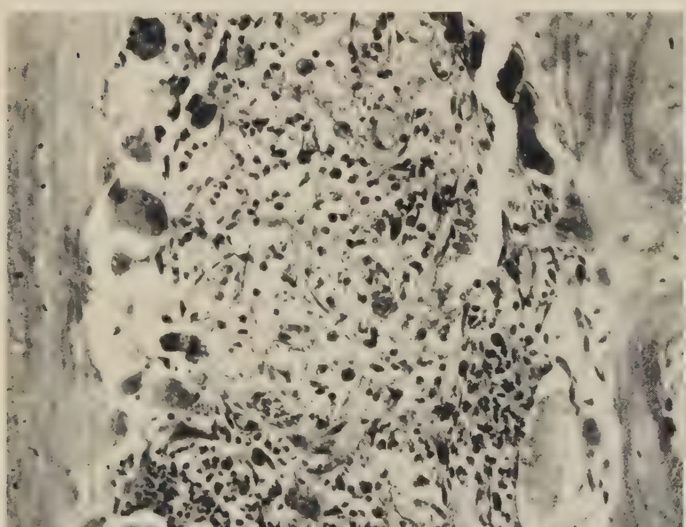
A. Early involvement of marrow with **phlebothrombosis of diploic veins** (from case at left). **B.** Pathway of infection to cranial cavity in patient with localized meningitis and multiple abscesses of frontal lobes. Purulent exudate fills marrow spaces; phlebitis of diploic veins; **purulent periostitis** with **extradural abscess** at right. (H. P. Mosher, Boston).



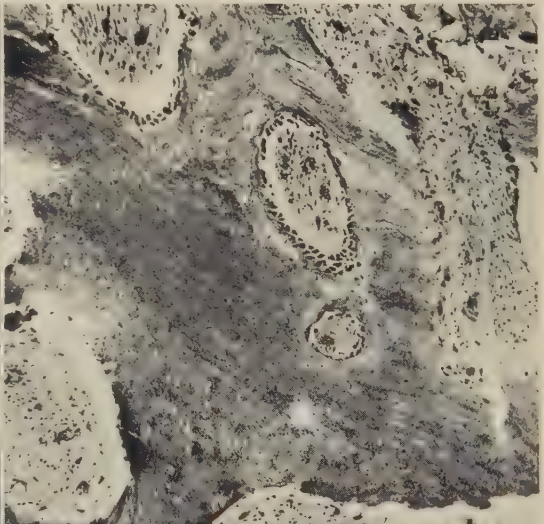
Frontal sinusitis and osteitis. Sinus cavity containing pus, at left. Active, extensive osteitis of outer table. At right, edema of overlying subcutaneous tissue of forehead, "Pott's puffy tumor." x 48. (H. P. Mosher).



Osteomyelitis of frontal bone. In this case, the infection eroded directly through the cortex into the subcutaneous tissue, and at operation considerable pus escaped from large subcutaneous abscess. x 48.

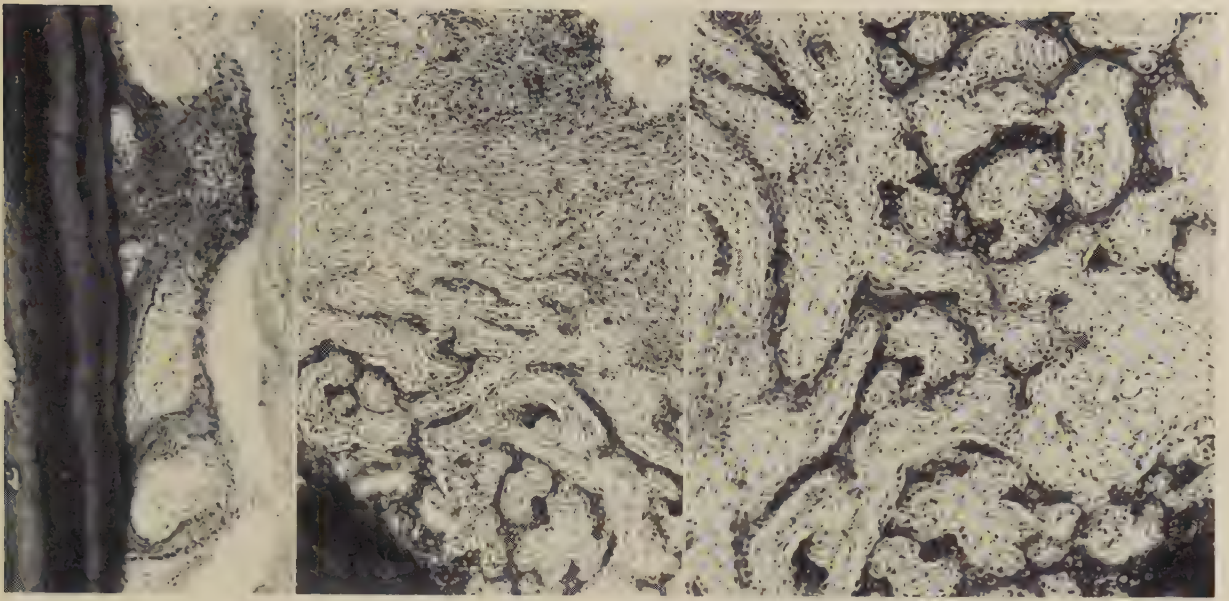


Osteomyelitis has stimulated osteoclastic activity with resulting ragged lacunae along both bony surfaces, and chronic suppurative reaction between. x 170.

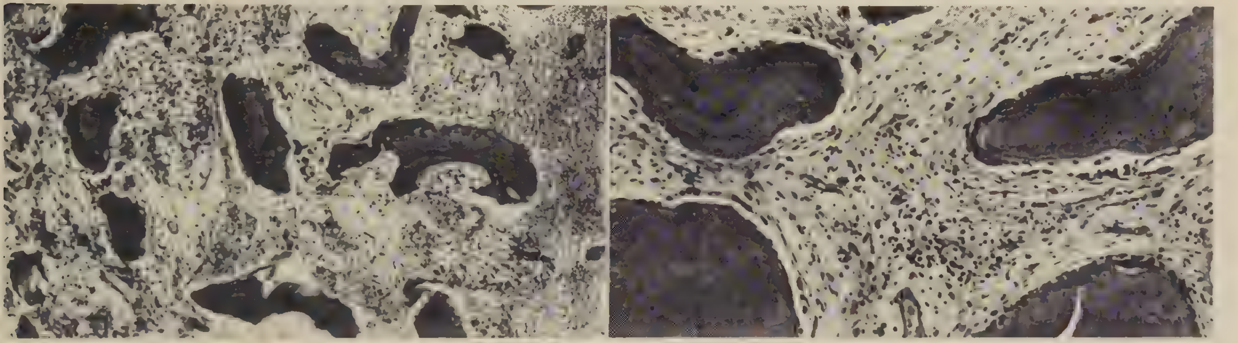


Severe osteitis and osteomyelitis with extensive bone destruction in another case of frontal sinusitis. This field shows both osteoclastic and osteoblastic activity, and chronic suppurative inflammation. x 62.

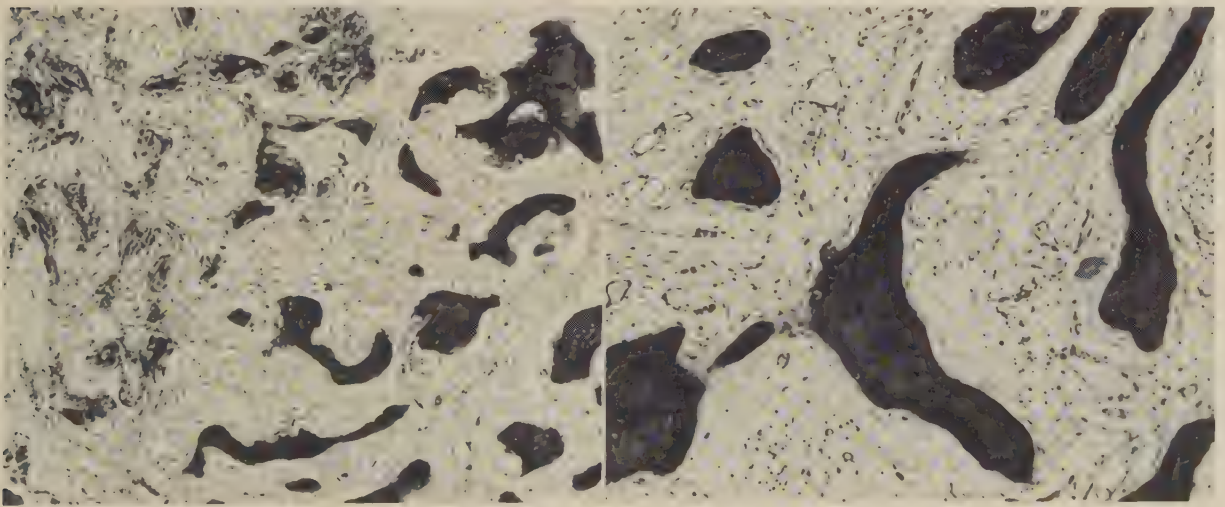
PERIOSTITIS AND REPAIR



Periostitis, extradural. Periosteal reaction following extension of infection from sinus may result in osteoid bone formation that thickens the cortical bone. A. Early extradural osteoid. x 75. B. More extensive periostitis in another case. x 48. C. Pattern at higher magnification resembles that of fibrous dysplasia. x 70.



Healing frontal osteomyelitis. Left, evidence of active infection still remains. x 70. Right, more advanced repair in same case. Fibrous tissue has replaced inflammatory tissue; bone trabeculae are outlined by osteoblasts. x 90.



Late phases of healing: Left, osteoid formation persists in left part of field; quiescent focus on right. x 55. Right, healed focus in same case. Fibrous tissue is denser and osteoblastic activity is absent. x 90. Histologic features such as these and in figure just above, may be found in cases of "fibro-osteoma" of the sinuses and skull.

CHAPTER 16

NASAL POLYPS

Nasal polyps occur with great frequency and are a manifestation of allergy, infection, or both in the nose and sinuses. An older concept was that the polyp was a true tumor, a fibroma or myxoma. The common polyp of the upper respiratory tract, however, is not a true neoplasm but a focal exaggeration of the polypoid type of rhinosinusitis, usually that induced by allergy. There is proliferation of connective tissue and of the vascular elements in the polyp, but it is an inflammatory reaction. Neoplastic proliferation of tissue elements presents clinical and pathologic pictures that readily differentiate it from the common polyp. These are the true fibromas, hemangiomas, and papillomas.

The development of polyps is largely a matter of vasomotor reaction and mechanics, the result of chronic and repeated attacks of inflammation of the mucosa. This process interferes with the drainage of interstitial tissue fluids and with the venous flow, producing edema and congestion. If the process is diffuse, polypoid hyperplasia results, and if it is localized sufficiently, a clinical polyp develops. The mechanism that causes interference with the flow of blood and fluids to and from the membranes is not clearly understood. The hypersensitivity of the mucosal vascular bed causes alterations in capillary permeability and an exaggerated response to local and reflex stimuli. The integrity of the stroma of the mucosa is altered by repeated wheal-like vasomotor reactions and prolonged edema, so that collagen fibrils are pushed apart and lose their stability. The accumulation of exudate, new blood vessels, and young connective tissue cells further increases the thickness of the stroma. Focal areas of the mucosa, because of their peculiar anatomic structure, respond more actively than others and result in local exaggerations of the tissue changes. Once such a nidus has developed, it is readily aggravated by hydrostatic pressure, by the action of gravity, and possibly by alterations in the chemical content of the tissue fluids.

Clinically, no predominant susceptibility has been noted in either sex. While nasal polyps are rare in children, a large percentage occur in young persons, particularly in those under 20 years of age. This probably reflects the importance of allergy as an etiologic factor.

Polyposis is more common in the upper part of the lateral nasal wall around the middle turbinate, especially in the middle meatus and in the ethmoidal region. This portion is an anatomic cross roads, and the mucous membrane in passing from the ethmoidal region, turbinate, and middle fossa undergoes considerable variation in the composition of its stroma, especially its vascular and glandular content. The common sites of origin of polyps are the middle turbinates and the mucosa of the ethmoidal capsule, but they also arise under the superior and middle turbinates, at the hiatus semilunaris and the infundibulum. These are favorable sites because the mucosal stroma is comparatively delicate, irritating discharges are common, and the closely approximated ridges exaggerate the interference to blood and lymph supply initiated by edema of the mucosa.

Polyps are solitary and unilateral or multiple and bilateral. In chronic allergic rhinosinusitis there is recurrent polyposis so that eventually dozens of polyps may fill both sides of the nasal cavity. Their appearance depends largely on the make-up of the stroma. Generally they are rounded or pear-shaped and translucent. In consistency they are usually soft and gelatinous and look like a mass of viscid mucus or the pulp of a skinned white grape. They are movable, do not bleed readily, and are insensitive to manipulation. The polypoid hypertrophy of the turbinates, however, is firmer, more sensitive to manipulation, bleeds more freely, and is sessile. The surface of polyps may be modified by hypertrophy of the epithelium or by ulceration, and their translucency is influenced by the extent of interstitial edema, vascularity, presence of hemorrhage, number of glands, presence of cysts, and amount of fibrosis.

The growth of polyps is accomplished largely by accumulation of interstitial edema and by development of true or false cysts rather than by proliferation of any of the tissue elements.

Microscopically, under the low power the striking feature of polyps is the looseness of the stromal structure. The delicate connective tissue cells and the fibrils are separated by clear fluid, more pronounced at the surface and decreasing toward the periosteal portion of the mucosa. The blood vessels are widely separated by this edema and they are further accentuated by the cellular exudate that surrounds them.

The surface epithelium is usually of the respiratory type, although in some areas it may lose its cilia, be reduced by abrasion to one or two layers of cuboidal basal cells, or undergo metaplasia to the squamous type. These changes are dependent on pressure or friction from surrounding walls, on direct trauma, or occasionally on bacterial infection. Exposure to irritating air currents and friction of long standing are the commonest causes of the squamous metaplasia. Occasionally, and particularly in polyps arising from the middle turbinate, there is a marked increase in goblet-cells. Some of these cells are on the surface, others are grouped as intra-epidermal glands, others are deep in the stroma. Such cells are active producers of mucin.

The basement membrane of the epithelial mucosa is usually obvious because of hyalinization, but the extent of this thickness depends on the chronicity of the process, and it is especially prominent if the polyp is on an allergic basis with recurrent exacerbations. The histogenesis of this membrane is described under chronic allergic rhinosinusitis.

The blood vessels may be widely dilated, particularly those near the surface where they have lost the support of the denser normal stroma. The larger arteries in the periosteal portion of the mucosa may show hyperplasia of the muscularis and can readily be distinguished from the young blood vessels developing in the outer portions of the polyp. The new vessels tend to radiate toward the surface instead of preserving the parallel course of the normal vessels.

Young fibroblasts, both of the spindle and stellate forms, are present in varying numbers. These and the young blood vessels, however, are not as prominent features in polyps as in other forms of chronic rhinosinusitis, nor is there the increase in stromal collagen that would be expected in connection with the development of the thick basement membrane. There is an associated increase in reticulin fibers that is not evident without silver impregnation.

The exudate consists predominantly of lymphocytes and plasma cells. Polymorphonuclear leukocytes are usually conspicuous by their absence. Eosinophils are present in varying numbers, depending upon whether the process is on an allergic basis and, if so, whether the reaction is at its height or in remission. The large mononuclear cell is not a prominent element, except as indicated in the description of the development of the basement membrane of the epithelial mucosa.

The number of mucous glands varies with the site of origin of the polyp. Those that arise from the maxillary sinus may contain a few, particularly if the polyps are in the mucosa near the ostium. The polyps originating from the ethmoidal sinus may not include glands. In some polyps, particularly those arising from the turbinates and maxillary sinus, the gland content is much greater than would be expected from inclusion of the elements normally present in the original mucosa. There is actual hyperplasia of glands, and this may form a striking feature of the picture.

Bone absorption and osteoporosis may accompany polypoid changes in the mucosa. These changes are particularly demonstrable in the middle turbinate. If there is an active pyogenic factor, there may be evidences of new bone formation. The pressure atrophy of the bony framework of the middle turbinate resulting from polyposis was formerly referred to as "necrosing ethmoiditis."

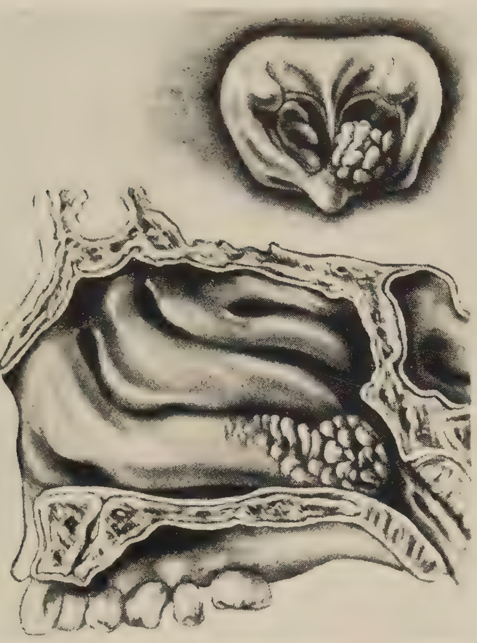
Choanal polyps (postnasal polyps) usually arise from the mucosa of a sinus and especially from the lateral wall of the maxillary sinus. Here the mucosa is extremely thin and more rudimentary than in other portions, and the blood supply and lymphatic drainage are more vulnerable. The lymphatic channels follow a circuitous course to the ostium so that any change in the latter may interfere with adequate lymphatic drainage. The edematous tissue pushes through the ostium of the sinus into the middle meatus of the nose, where it lies along the floor and presents far back in the posterior choana. These polyps are usually rounded or pear-shaped and have a long stalk. The smooth, glistening, grayish white surface can easily be differentiated from the pebbled, mulberry-like, hyperplastic, polypoid reaction of the posterior turbinal tips.

As a rule, choanal polyps are unilateral, especially if they are on an infectious rather than an allergic basis. Removal of the infectious polyp and drainage of the sinus usually constitute adequate treatment. If allergic, they are usually bilateral, the sinus mucosa is the site of generalized polyposis, and the sinus cavity may be filled with polyps and swollen mucosa.

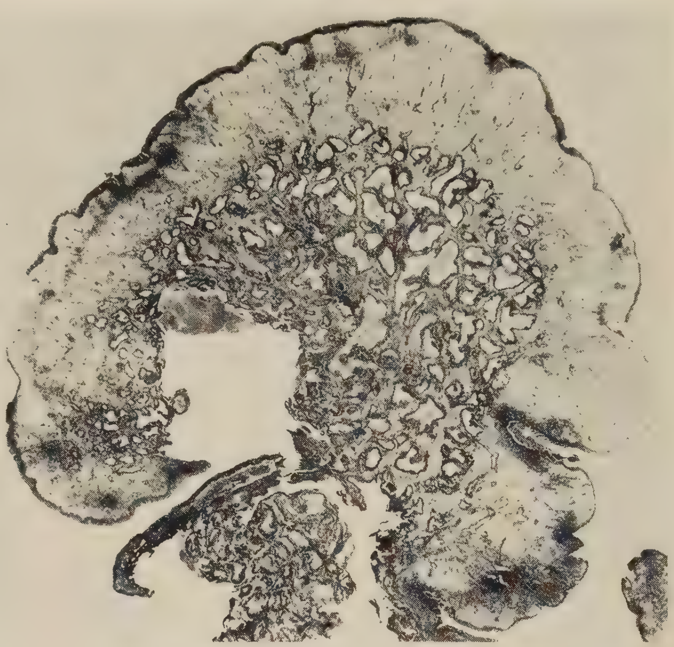
The treatment of polyps depends on the etiology and to some extent on the site of origin. Those that develop from the turbinates can be completely eradicated by simple removal with the inclusion of some surrounding mucosa or the tip of the turbinate. Those, however, that arise in a sinus and are usually choanal in position will recur following simple removal of the intranasal portion because the pedicle is still contained within the sinus and the sinus mucosa is usually the seat of polypoid hyperplasia. Radical sinus operation may be necessary, therefore, to obviate recurrences of the polyps.

Polyps that develop from allergic reactions do not respond to local treatment alone, but the underlying allergy must be relieved by desensitization or by the patient's avoidance of exciting antigens. Since those of infectious origin may be successfully treated by surgical removal, a correct diagnosis is of great importance. Recognition of allergy as a potent factor in the etiology of polyposis has done much to discourage the radical operations formerly relied on to prevent recurrences.

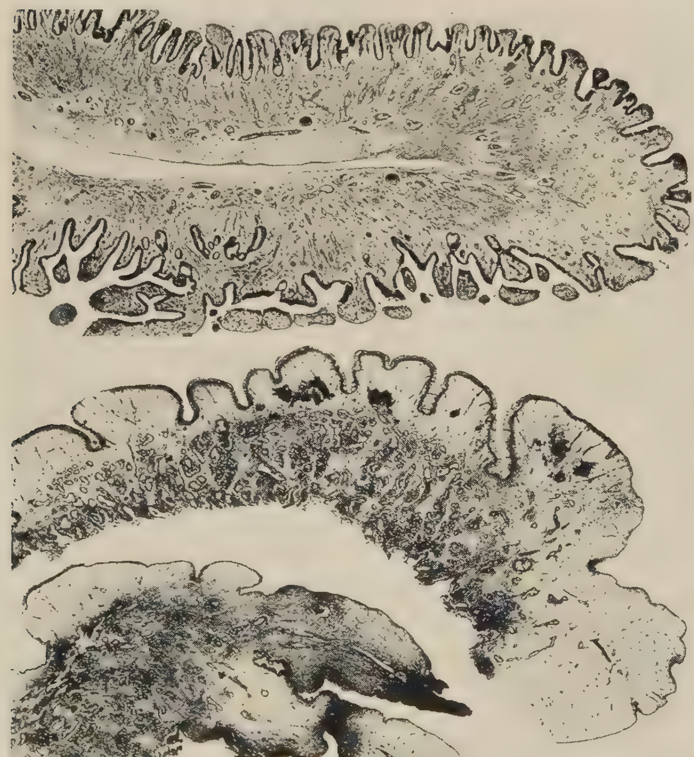
POSTERIOR HYPERTROPHY OF INFERIOR TURBINATE



"Mulberry" (polypoid hyperplasia of) turbinate. Drawings of the clinical appearance in the most frequent site of involvement, the posterior part of the inferior turbinate.

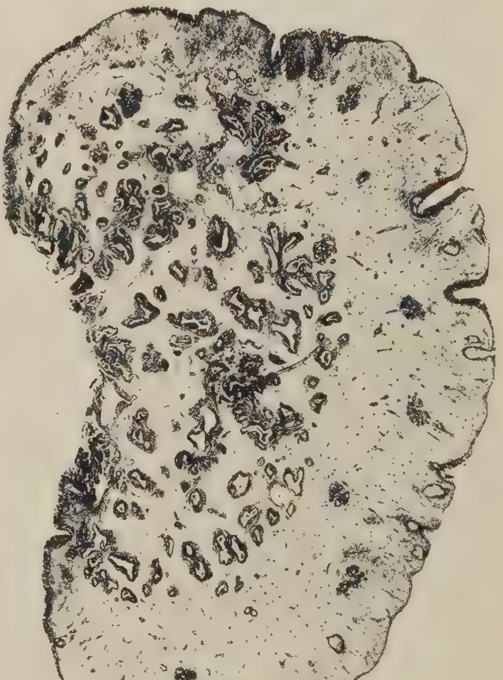


Histologic features. Polypoid turbinal mucosa sectioned parallel to bony attachment. Superficial stroma edematous; deeper stroma denser. x 8. Hyperplastic cavernous plexus is not infrequently diagnosed hemangioma.



Surface configuration of hyperplastic turbinate:

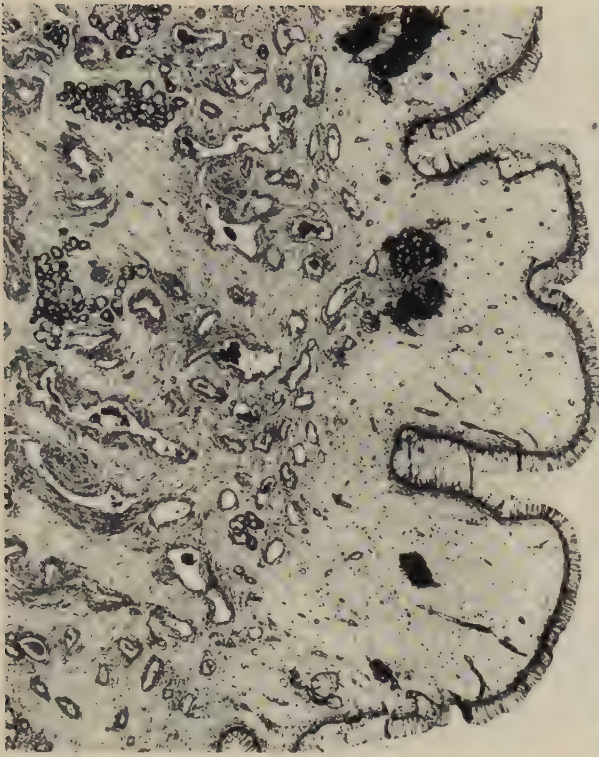
A. Finely papillary posterior tip that caused partial nasal obstruction. x 9. **B.** More coarsely papillated type from another case. x 8.



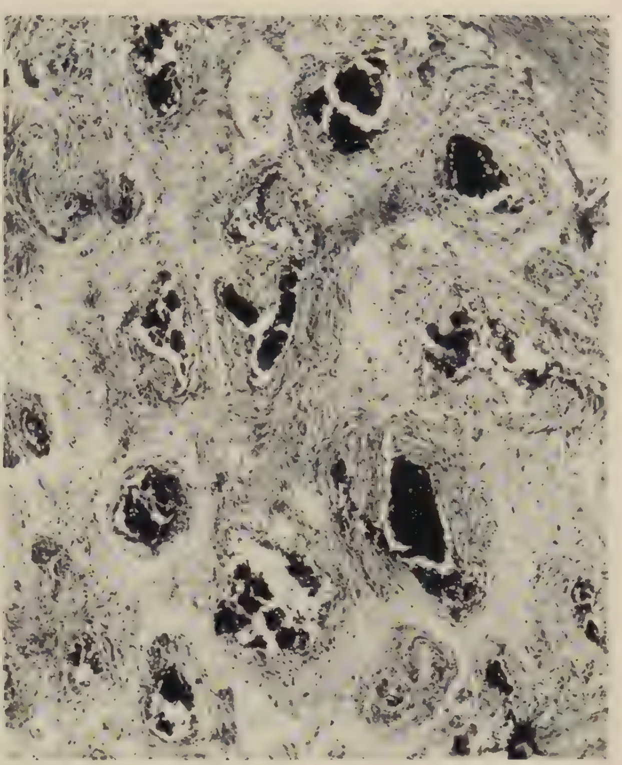
Polypoid, relatively smooth-surfaced mass which is diffusely edematous. Many blood vessels in deeper stroma. x 10.

CHRONIC RHINITIS

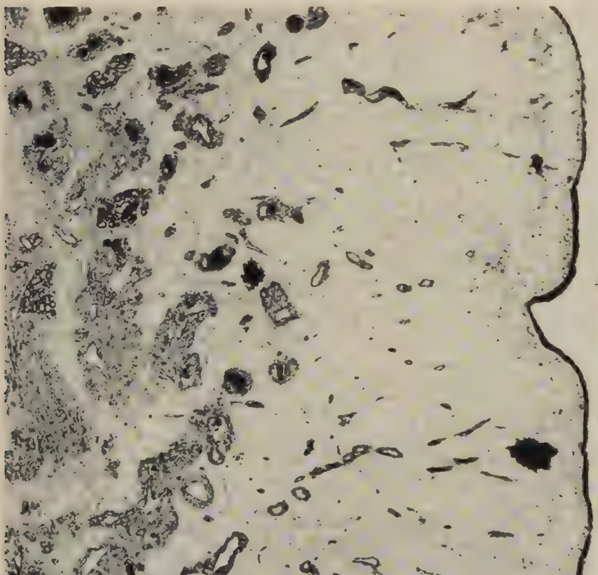
HISTOLOGIC DETAILS OF "POLYPOID TURBINATES"



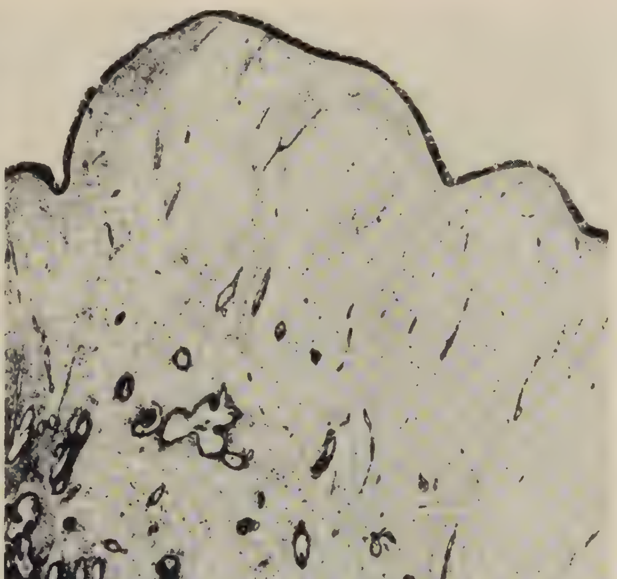
Low papillary configuration of surface; epithelium almost entirely of goblet cell type; edematous superficial stroma; dilated lymphatics; practically no cellular exudate. x 33.



Cavernous vessels are congested; surrounding stroma is dense. No evident periphlebitis. x 62.

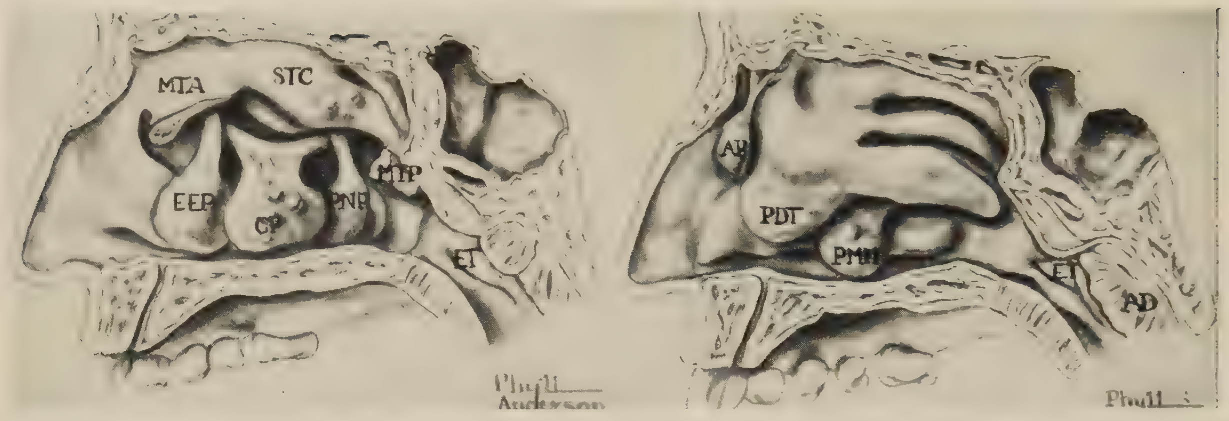


Diffuse edema, but little exudate; proliferation of capillaries, and prominent cavernous plexus. x 24.

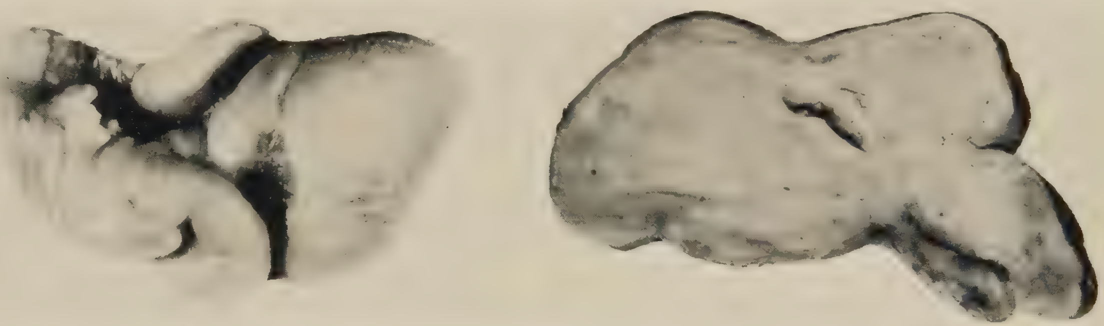


Radial arrangement of new capillaries—perpendicular to surface. x 33.

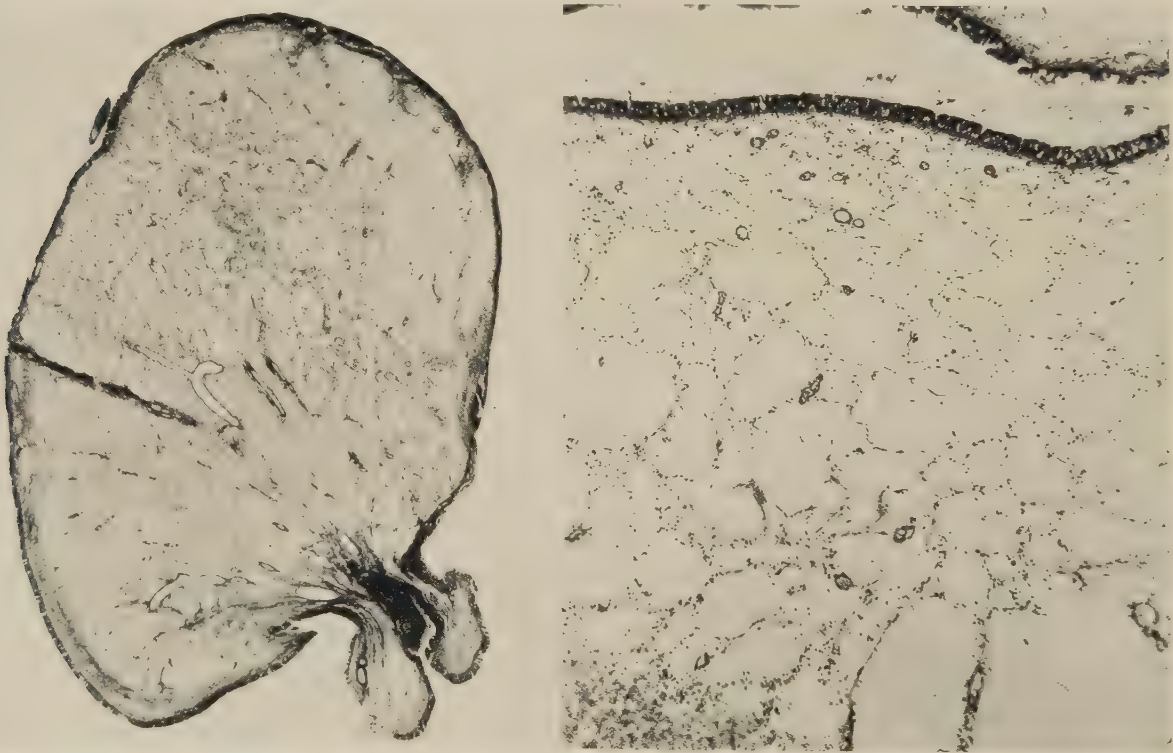
CHRONIC HYPERPLASTIC RHINITIS
WITH NASAL POLYPS



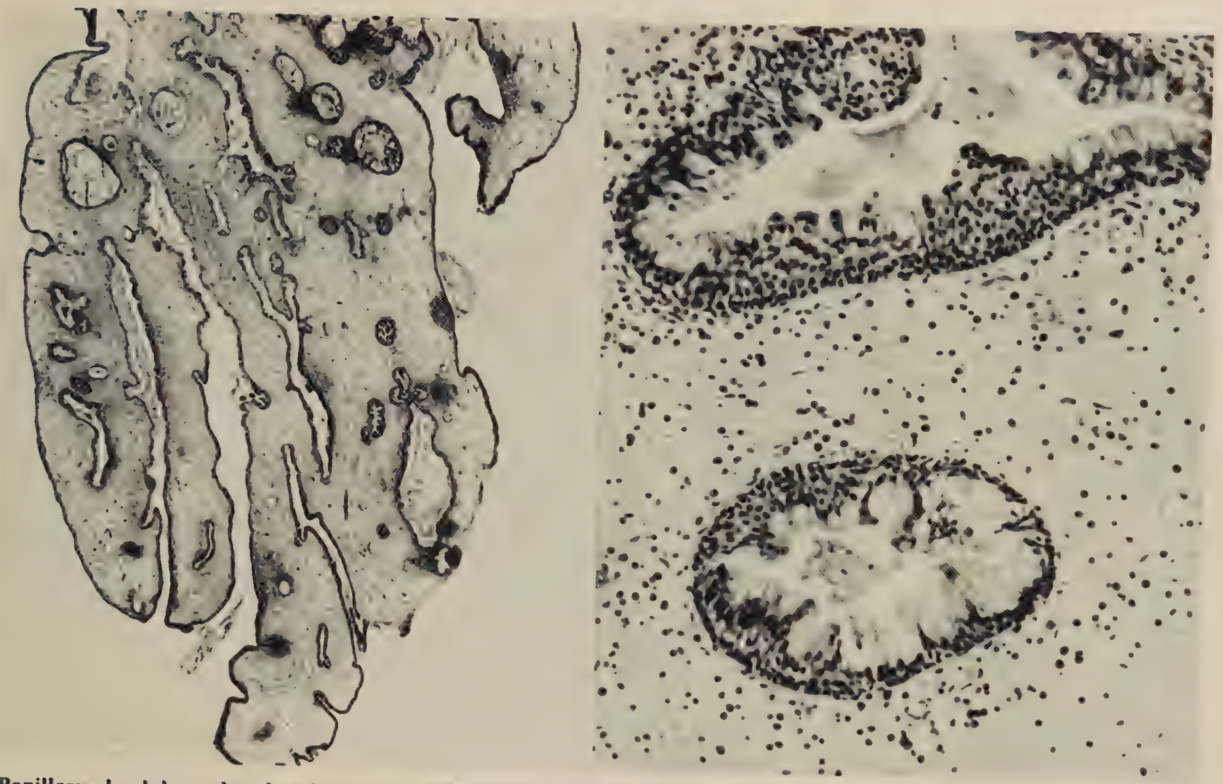
Possible sites of polyp formation, lateral wall of nasal cavity. Middle turbinate (MTA, MTP) removed in drawing at left. AP and EEP–anterior ethmoid region; CP and PMM–polyps middle meatus; PDT–middle turbinate; STC–superior turbinate; PNP–posterior nasal cavity. (Semenov).



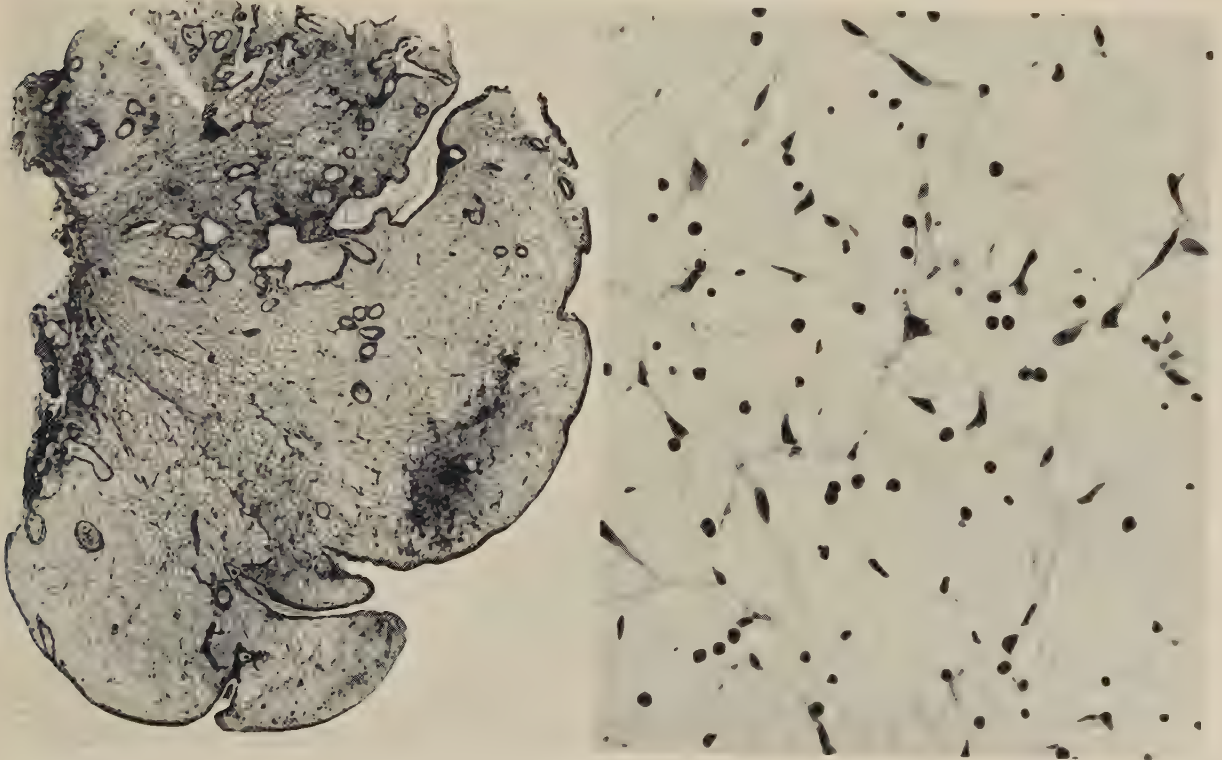
Gross features of two polyps, slightly enlarged: left, lobulated polyp with intact epithelial surface; right, smooth, homogeneous cut surface of moderately firm polyp.



Histologic features of edematous pedunculated polyp. Squamous metaplasia of portion of surface epithelium. Scant, diffuse cellular infiltration with a few focal collections of cells, most prominentt in subepithelial location, at left. x 10. Diffusely edematous stroma giving a lacy appearance. x 61.

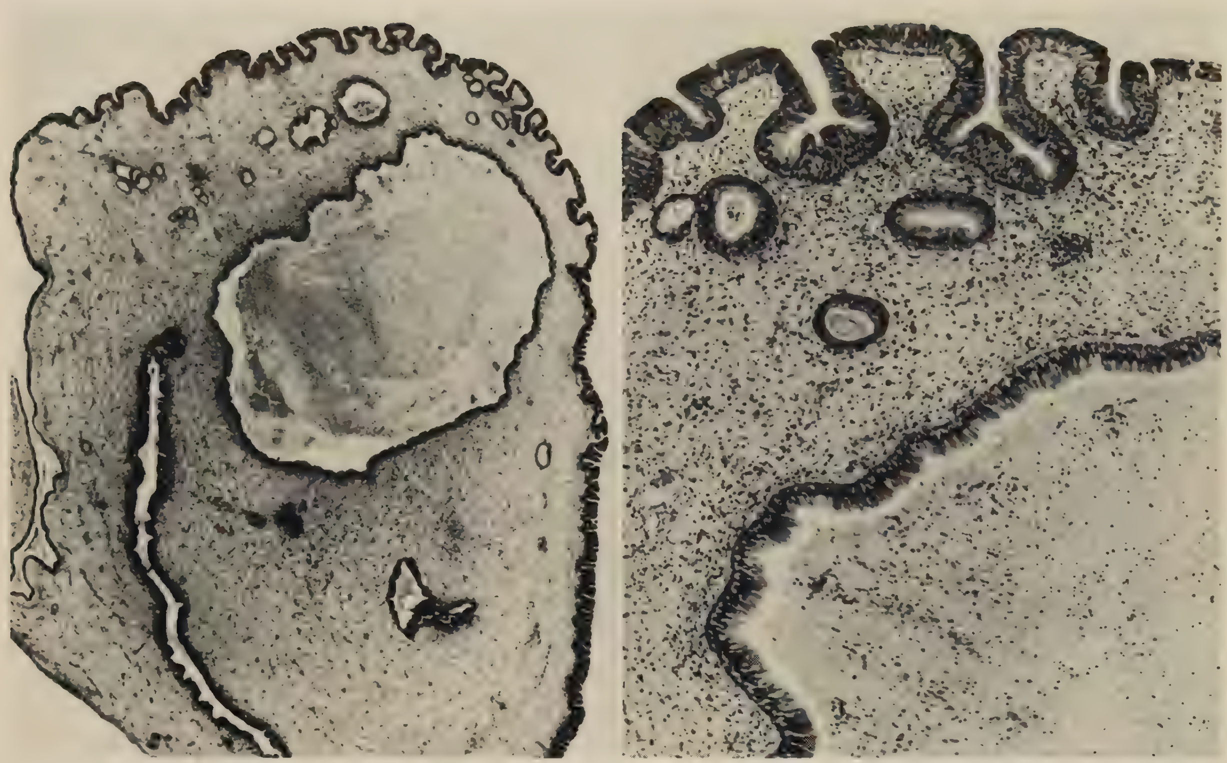


Papillary glandular polyp. In addition to the lengthening of preexisting gland ducts, invagination of the surface epithelium has resulted in a papillary architecture and has produced pseudoglands. x 8. Hyperplastic lining of duct or modified surface epithelium at top; in cross section, at bottom. *Edematous stroma.* x 90.

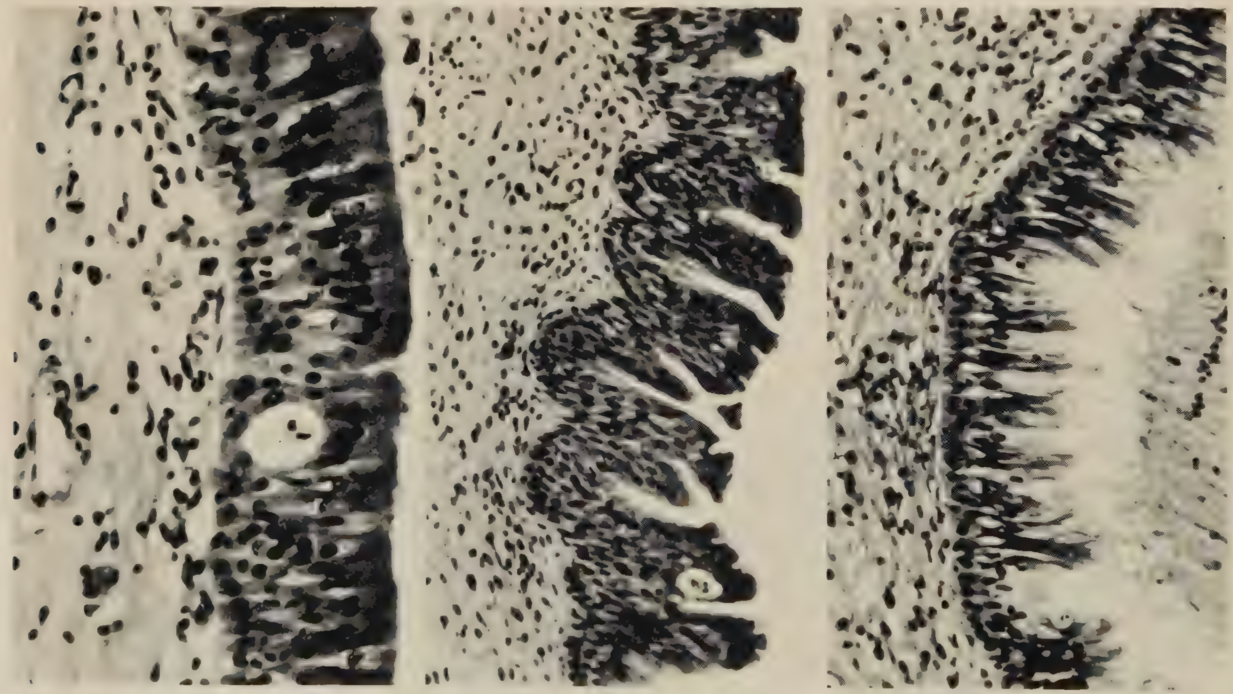


Myxomatous glandular polyp. Polypoid mass with glands, some of which may be dilated remnants of preexisting glandular structures. Others appear to be pseudoglands produced by invagination of surface epithelium. x 9. *Fibromyxomatous stroma* with stellate and spindle-shaped cells which have delicate processes. Scattered inflammatory cells. x 220.

CYSTIC

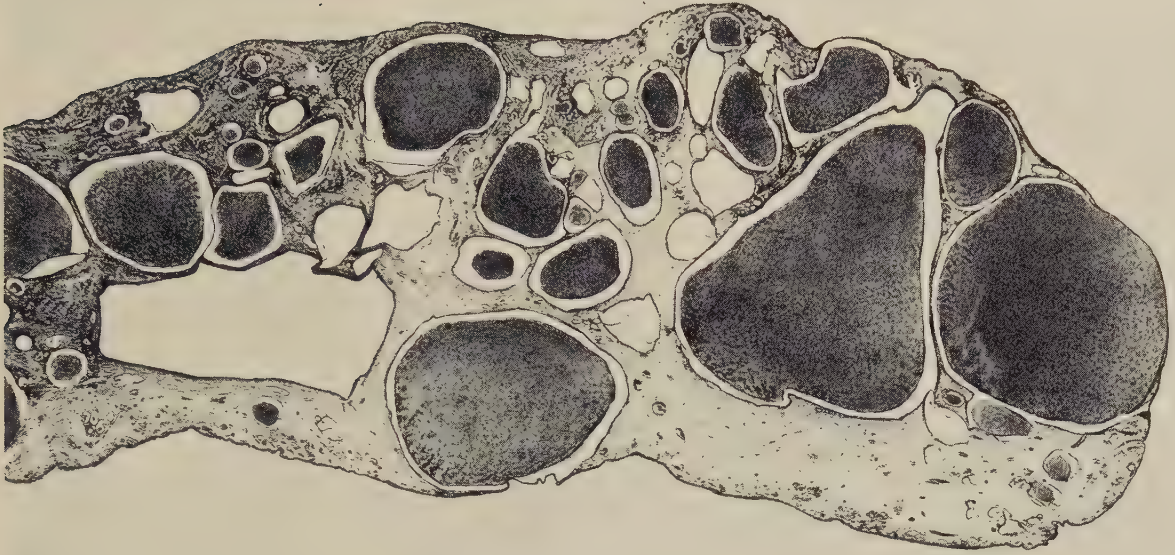


"Cystic" nasal polyp probably due to infection. True retention cyst produced by obliteration of duct in the inflammatory process, a common feature in chronic polypoid rhinosinusitis. x 16. Magnified field at right shows active production of mucus by epithelium of cyst; hyperplastic "corrugated" surface epithelium; rather *cellular fibromyxomatous stroma* diffusely infiltrated by leukocytes, chiefly lymphocytes. x 70.

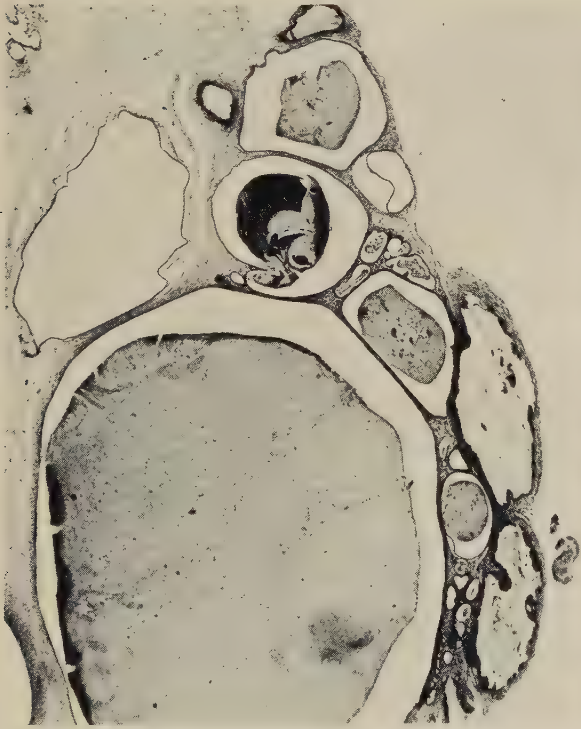


Types of epithelium in polyp shown above. Left, "oncocytoid" change present in one glandular structure. Non-ciliated epithelium with strikingly eosinophilic cytoplasm and distribution of nuclei reminiscent of ducts in major salivary glands. x 300. Center, saw-toothed, modified respiratory epithelium at surface. Goblet cells in deeper portions of tiny crypts. x 145. Right, epithelium of cyst with partial "mucinous transformation." x 205.

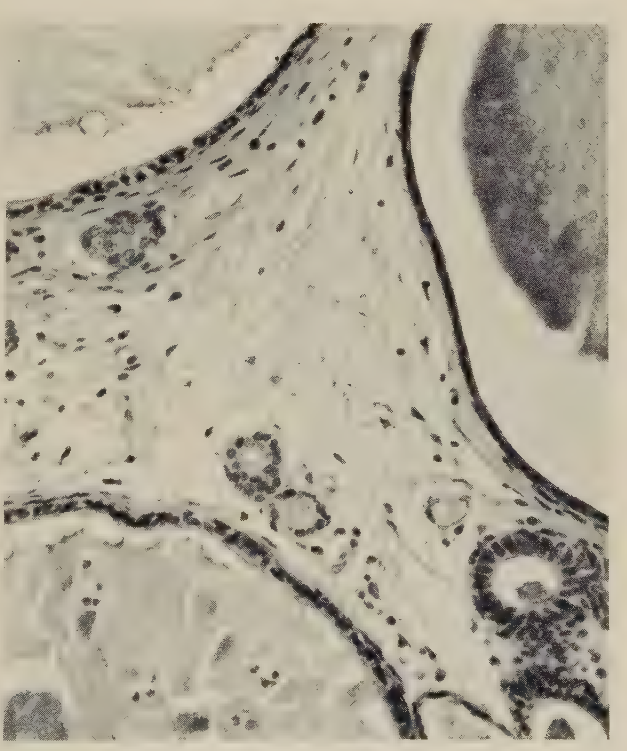
CYSTIC, GLANDULAR; PSEUDO-ADENOMATOUS



Striking pseudo-adenomatous pattern has been produced by the cystic dilatation and enlargement of many of the numerous glands within the polyp, which has a *cellular fibrous stroma.* A large solitary polyp attached to the spheno-ethmoidal area of a young man who had had symptoms of unilateral nasal obstruction for only 3 months. x 10.



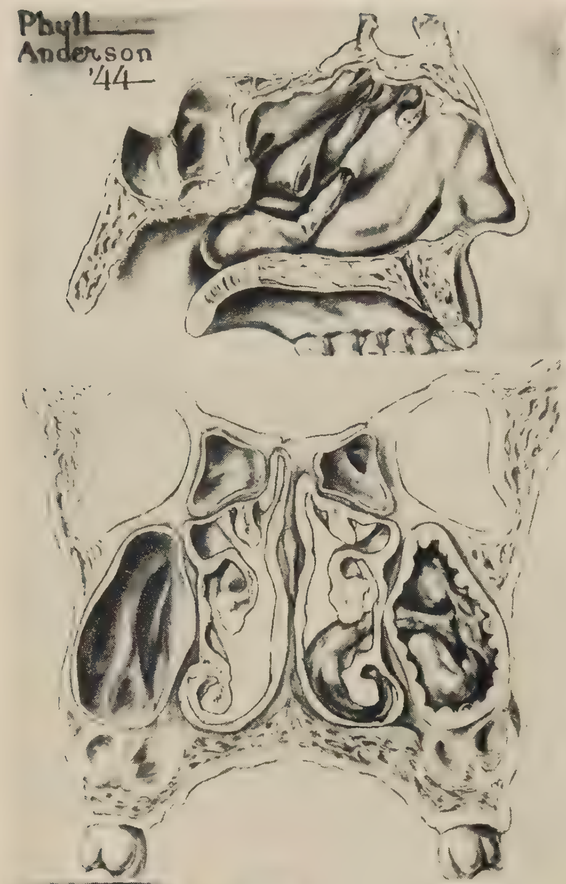
The multiple cysts contain mucinous secretion, parts of which appear stringy and fluid, others inspissated. x 24.

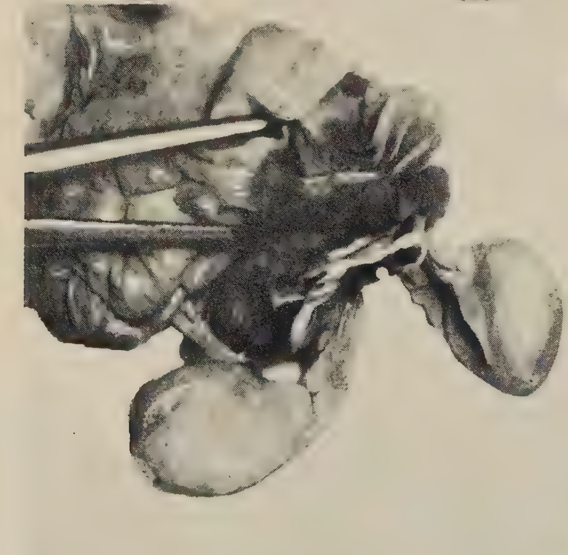


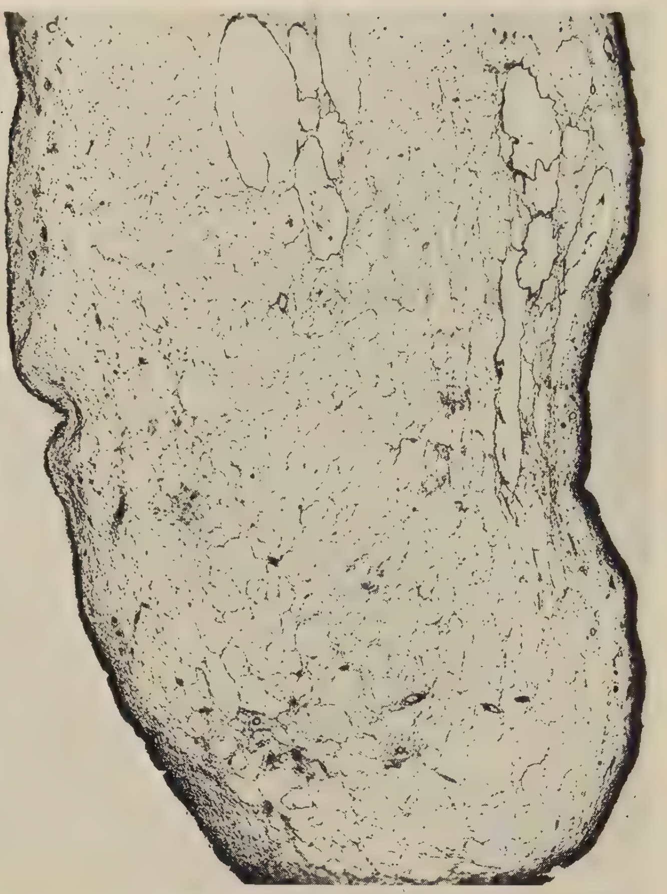
Epithelium of cysts varies from tall columnar and cuboidal (left) to flattened cells (right). The fibrous stroma is edematous. x 275.

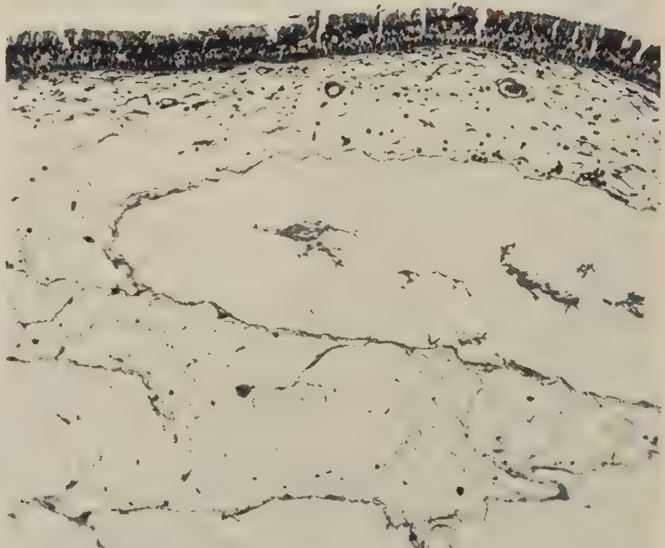
ANTROCHOANAL POLYPS

(CHOANAL POLYPS)







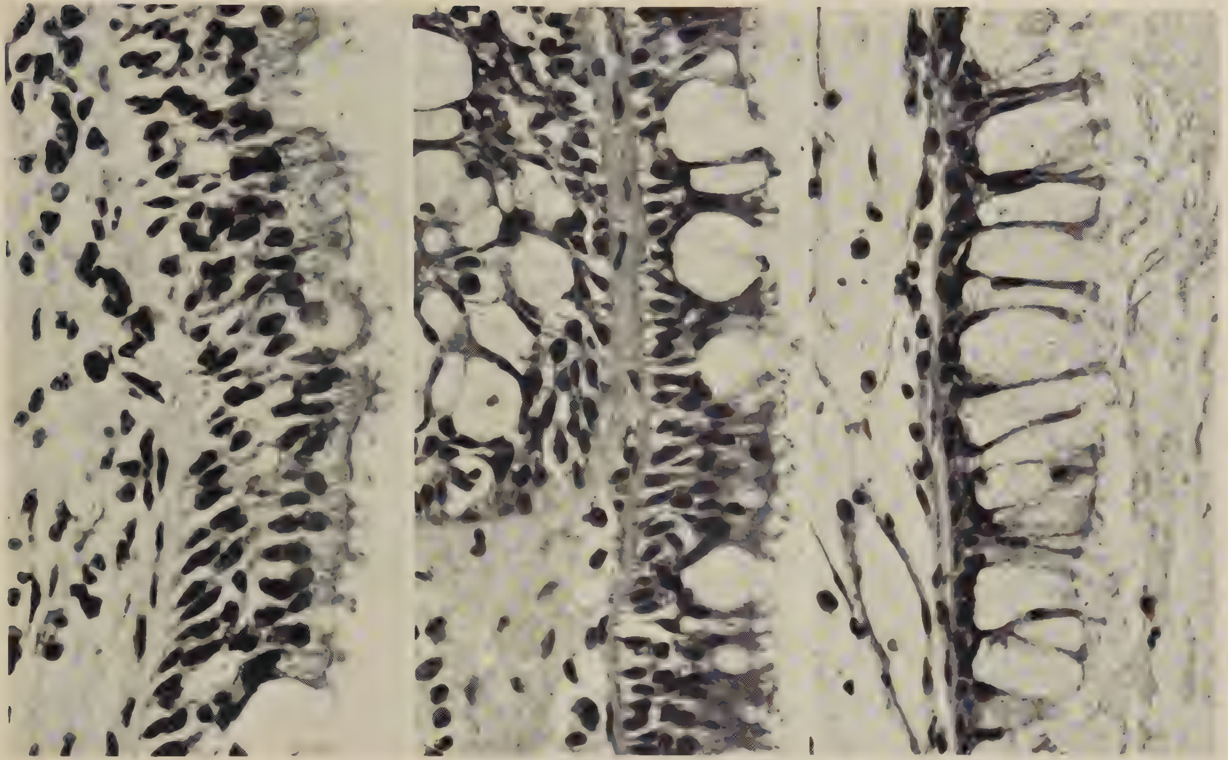


Antrochoanal polyp. Drawings illustrating origin of this polyp from antral mucosa. It emerges through the ostium, and, as it elongates, extends to and through the choana. Unilateral polyps, such as this, appear more frequently to be due to infection than to allergy. (Semenov.)

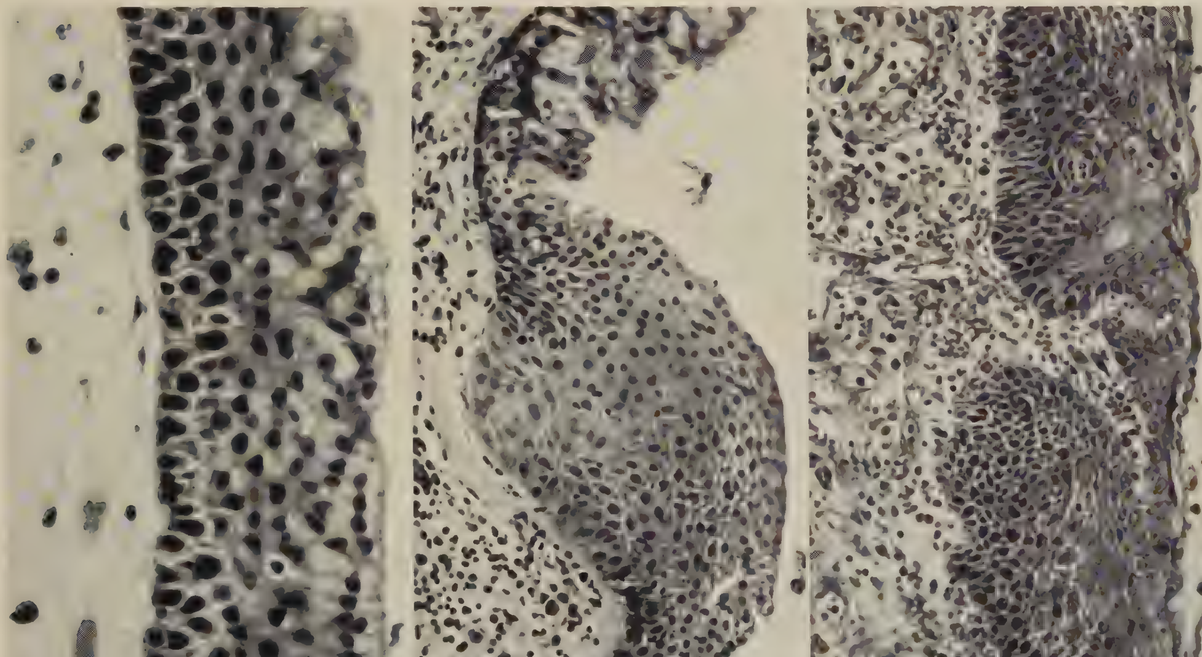
Gross specimen includes antral mucosa and antral polyp as well as choanal polyp (left at bottom).

Histologic features. The polyp has a very lacy edematous stroma with "interstitial cysts." Vessels and exudate are not as prominent as in the allergic polyp. x 16. Much of the epithelium lacks cilia but has retained its respiratory character; basement membrane is distinct, but not thickened; pseudocystic interstitial spaces in edematous stroma. x 75.

EPITHELIAL CHANGES



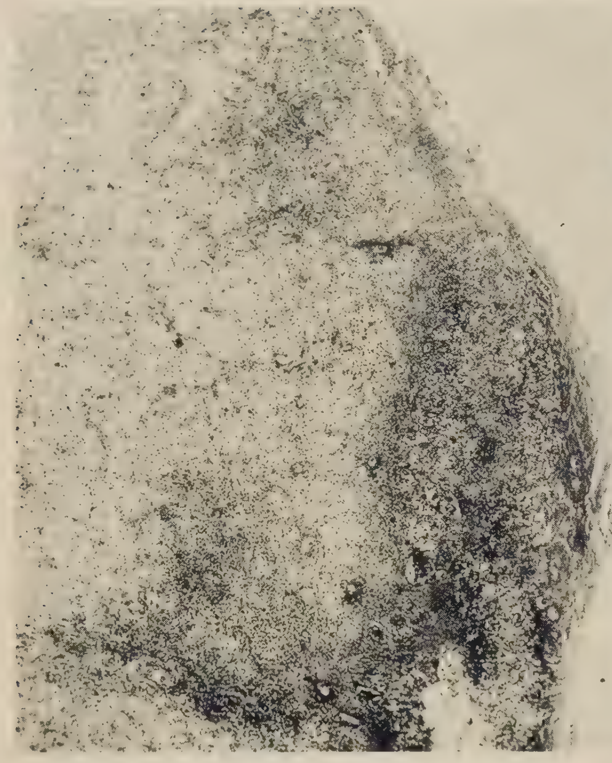
The epithelium covering polyps undergoes a wide variety of changes, tending either toward the glandular or squamous types. A. Relatively normal respiratory type with cilia retained. x 450. B. Several intra-epithelial mucous cysts. x 400. C. Predominantly goblet cells with heavy mucus production. x 400.



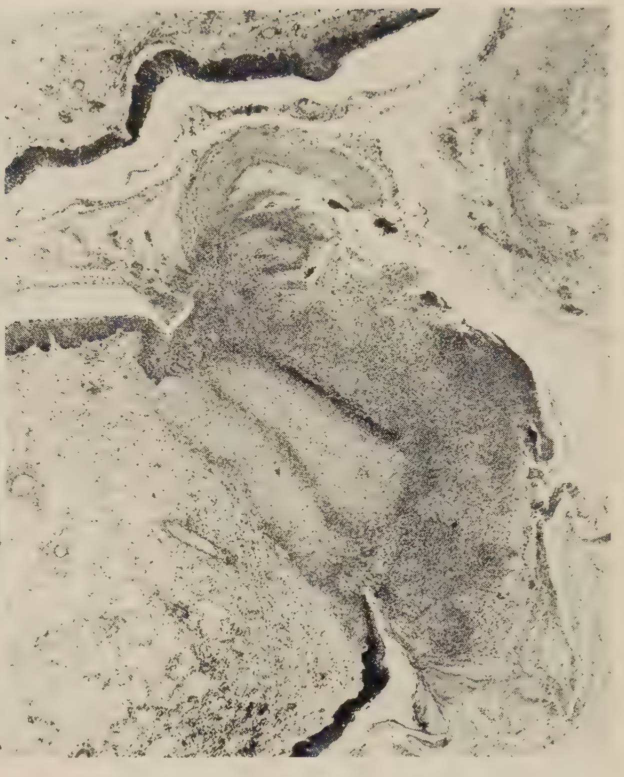
In these three the change is toward the squamous. D. Loss of cilia and stratification of nuclei. x 395. E. Broadening out of cells to squamous type. Note sharp demarcation of the two types. x 165. F. Squamous epithelium showing dyskeratosis. Frank malignancy, however, is very rare. x 185.

NASAL POLYPS

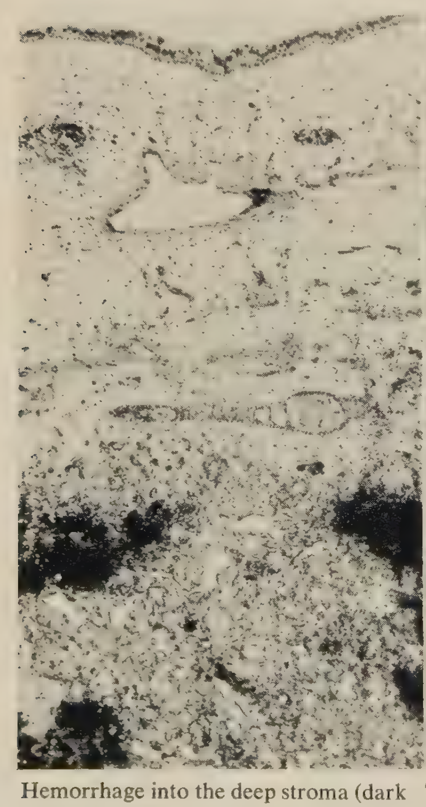
HISTOLOGIC VARIATIONS



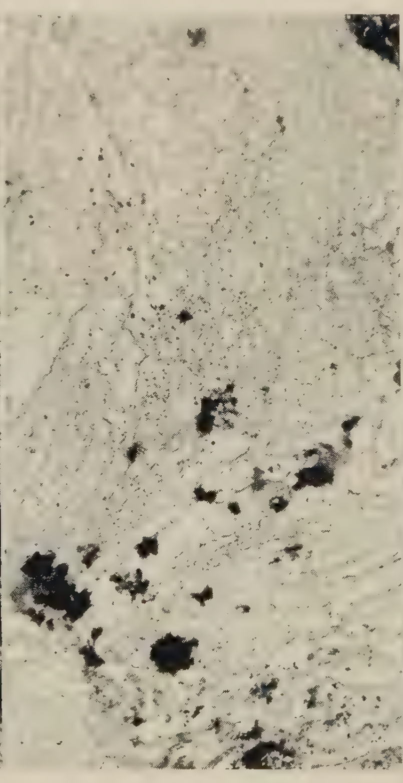
Heavy exudate and granulation tissue in an ulcerated polyp. If the surface of the polyp is not ulcerated, purulent exudation is absent. x 48.



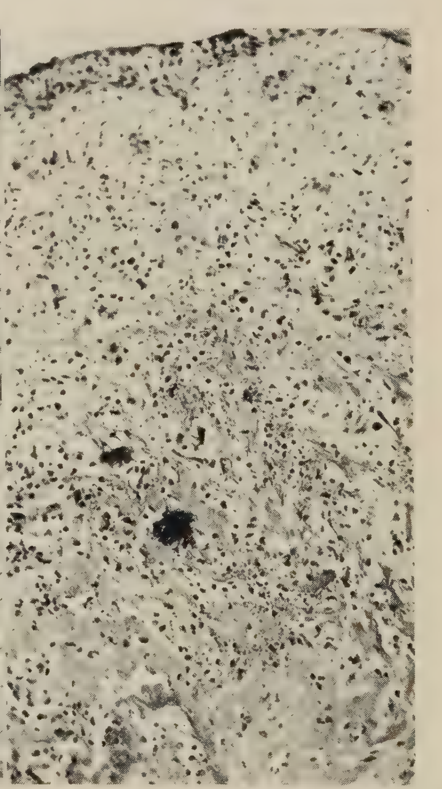
Ulceration of "kissing" surfaces and protruding masses of exudate resulting from friction of two adjoining polyps. The epithelium has undergone squamous metaplasia. x 40.



Hemorrhage into the deep stroma (dark areas) with organization. x 75.



The black spots are calcified areas in an old hemorrhage. x 125.



Masses of fibrinoid material have accumulated in the stroma. x 125.

CHAPTER 17

SPECIFIC INFLAMMATORY DISEASES OF THE NOSE

Atrophic Rhinitis (Ozena, Rhinitis Sicca).—Ozena was established as a clinical entity in 1876. The syndrome consists of atrophic changes in the nasal mucosa and frequently in the turbinate bones, resulting in abnormal patency of the nasal passages, the formation of crusts, and the throwing off of an offensive, fetid odor. Anosmia practically always results. There are frequent reports of familial distribution. The Negroes of Africa and the Southwest Pacific islanders are free of the disease, Central and South Americans suffer from it, and the yellow races seem particularly prone to it. It is five times as frequent in the female as in the male. There seems little doubt that it begins in childhood, but the typical syndrome is not well developed until young adult life. These facts seem to argue that there must be basic intrinsic conditions, as well as the more obvious infectious episodes of childhood, responsible for the syndrome. Numerous theories have been advanced as to what these underlying factors might be, and they can be categorically listed as follows:

1. The end stage of any rhinitis or sinusitis (Pollock);
2. A neurogenic result of injury in the region of the sphenopalatine ganglion;
3. A disturbance of the nasogenital relationship;
4. Cranial dysplasia from hypopituitarism;
5. Infection caused by a specific organism, particularly *Klebsiella.* Incidentally the Perez bacillus that has been frequently isolated from the nose and was thought to be the cause is most likely a secondary contaminant and, at best, only partially responsible for the putrefaction;
6. Primary endarteritis or periarteritis of the terminal arterioles (Eggston);
7. A direct effect on the mucosal blood vessels by estrogenic hormones secreted by the pharyngeal pituitary (Ruskin);
8. Related to polyendocrinism (Patroni);
9. A combination of several of these factors (Thornell).

There are still, however, those who consider the syndrome simply a sequel of rhinitis or sinusitis in childhood, irrespective of cause, be it diphtheria, any of the exanthems, influenza, or allergy, as long as it results in purulent sinusitis. It would seem reasonable that in spite of the definiteness of the clinical syndrome, the etiology is not the same in every case.

The incidence of the disease has decreased in recent years and this has been attributed to the better nutrition and medical care that children receive. The obvious relationship of childhood infections to the disease is a good argument for a careful nose and throat regime for children that will prevent the establishment of chronic purulent rhinosinusitis. Such chronic condition can lead to structural and physiologic alterations in the nose that make it vulnerable to more serious diseases.

Myles divided the clinical course into three stages: (1) mucopurulent rhinosinusitis, (2) incrustation and fetid odor in adolescence, (3) atrophic phenomena as the persistent adult stage.

The atrophic changes are not always distributed uniformly. They can be evident in one nostril and not in the other, and there may be a variation in the extent of atrophy in the individual bones of one nostril. The inferior turbinate is usually the first affected. Wingrave considered the small size of the turbinates not the result of secondary atrophy but of retardation of growth by the childhood infection. He could find no specific changes in the bones so far as osteoclastic and osteoblastic activity were concerned. Eggston, however, claimed that "condensating osteitis" of the bony walls of the sinuses is common. He was impressed also with the striking reduction in lymphatic tissue, including the tonsils, and considered it a significant feature of the disease.

Grossly, in addition to the roomy nasal cavities and the reduction in size of the turbinates, the mucosa is dry and abnormally smooth where it is not covered with crusts. Incidentally, the mucosa usually loses its "tickle" reflex.

Microscopically, the epithelium is greatly reduced in thickness; much of it, including the olfactory epithelium, has changed to the squamous type, and those cells that have retained their columnar form have lost their cilia. There is atrophy of the mucosal glands and particularly of the serous-secreting elements. Such mucus as is secreted, therefore, is very viscid. This is largely responsible for the development of the crusts. The basement membrane of the mucosa is thick and hyalinized.

In the earlier stages the mucosa may be thickened by exudate and edema. Later the edema disappears and the cellular exudate made up chiefly of lymphocytes and plasma cells, but with a larger content of polymorphonuclear leukocytes than is usual in ordinary rhinitis, tends to concentrate about the glands and blood vessels. The deeper blood vessels in the earlier phases exhibit marked hyperplasia of the muscularis; but as the condition progresses all of the vessels show more or less obliterative changes, consisting of intimal proliferation and fibrosis of their walls. There is progressive fibrosis of the stroma and, finally, scarring. The atrophy of the mucosa, including its glands, and the loss of ciliated epithelium seriously alter the physiologic activity of the nasal cavities. The inspired air is improperly warmed and moistened and this leads to secondary changes in the nose itself and in the pharyngeal mucosa.

In spite of the possibility that the small size of the bones may be in part, at least, the result of arrested development, the turbinates do show rarefaction in some instances.

In general, two types of the disease are recognizable: (1) secondary atrophic rhinitis due to infection, and (2) primary atrophic rhinitis or ozena which Ruskin considers due to changes in the blood vessels with little evidence of infection. In the secondary form he found rarefaction of the underlying bones, but in the primary type they were definitely sclerotic.

In regard to the first group, Semenov and others have noticed that over-ventilation of the nose resulting from radical surgical treatment, particularly when it includes the removal of the gland-bearing turbinates, leads to significant epithelial changes, particularly metaplasia, and to excessive drying of the mucosa. The clinical picture can simulate ozena, including the presence of pus, odor, and crusts.

There is no conclusive evidence that the use of steroids of either the male or female hormonal groups is more than temporarily effective in the treatment of ozena.

Rhinitis caseosa (rhinitis cholesteatomatosa, caseous purulent rhinorrhea) is a rare disease characterized by an accumulation in the nose of an extremely offensive cheesy mass accompanied by a seropurulent discharge that finally results in intranasal and extranasal deformities. The usually accepted explanation is that the condition is secondary to nasal stenosis with accumulation of exfoliated epithelium and secretion, and subsequent putrefaction of this material. It is most common in the third and fourth decades of life, particularly among the French and Italians. It has been called nasal cholesteatoma and shows the same eroding effect as cholesteatoma of the temporal bones.

Myersberg, Bernstein and Mezz made a comprehensive survey of the condition and found that it is invariably unilateral and is somewhat more frequent in males. It begins with clinical evidence of chronic suppurative sinusitis, including the presence of polyps, or the nostril may be occluded by a foreign body. There is a mucopurulent discharge that later becomes more profuse and extremely offensive. The nasal cavity is filled with a cheesy mass; the ethmoid, turbinates, and naso-antral wall are more or less eroded and the septum is deflected. At this stage the patient is usually suffering from the effects of a complicating involvement of the lacrimal sac, evidenced by conjunctivitis and tearing. In neglected cases the bones may be eroded to the extent that there is deformity of the face, and fistulae have opened onto the skin surface and into the mouth. The resulting cavity is filled with the purulent cheesy material. In this advanced stage rhinitis caseosa can be mistaken for an invading malignant tumor.

The pathologic changes are not specific. The cheesy mass is made up of necrotic tissue, largely keratin from the squamous epithelium and more or less exudate, harboring a miscellaneous assortment of bacteria and fungi. The tissues are the seat of a chronic suppurative necrotizing process and often contain cholesterol clefts, with or without associated foreign body giant cell reaction.

In spite of the startling clinical picture the condition seems amenable to simple surgical care.

Scleroma (Rhinoscleroma).—von Hebra first described rhinoscleroma in 1870 and considered it a form of cancer. It is a chronic granulomatous inflammation involving the nose, nasopharynx, and less frequently the larynx and trachea. One-third of the cases show involvement of the nasopharynx, soft palate, and uvula. The endemic centers are Egypt and Eastern Europe. It is also common in South and Central America and in the Dutch East Indies. About 100 cases have been reported in the United States and Canada, and it is probably more frequent here than this figure would indicate. Semenov states that it is common among the Mexicans in Los Angeles. Of historic interest was the discovery among the material in the Medical Museum of a larynx from a young male colored resident of Washington, D.C., contributed in 1904. Microscopically the lesions could be identified as scleroma. The condition is seen most commonly in early adult life and there is a slight preponderance of females. It is not observed among those who live under good hygienic conditions.

Even though the gram-negative diplobacillus, *Klebsiella rhinoscleromatis,* or von Frisch bacillus, is always present in the lesion, it has not been definitely proved to be the cause, for it also is found in the healthy nasal mucosa. Possibly a symbiotic virus is also involved. There is some histologic and clinical similarity between rhinoscleroma and granuloma inguinale, especially as the latter is seen in females, and an etiologic relationship is suspected. The disease is not highly contagious.

The process confines itself to the soft tissues. Cartilage and bone are not affected. This is a point of some importance because it can be confused with carcinoma, which will, of course, invade all tissues. In the early stages it may be confused with atrophic rhinitis and later with syphilis and tuberculosis. The complement fixation test has been claimed by some to be diagnostic (Levine et al.) but its usefulness is doubtful. Biopsy should be utilized for diagnosis.

Clinically the disease is divisible into three roughly defined stages: (1) exudation, when there is profuse brownish nasal discharge with crust formation, (2) proliferation, in which dark red nodular masses form in the nasal mucosa, (3) cicatrization, with contraction and deformities of the affected parts.

The disease begins as a small flat nodule, usually on the nasal septum. In the course of months or years it spreads either as multiple discrete nodules or as a diffuse involvement of the mucosa. These masses are pale and have a characteristic cartilaginous consistency. Ulceration is not a feature. The obliteration of the nasopharynx and the deformities of the lip and palate are the result of severe scarring contractures. The disease is very slowly progressive and may last for 20 or 30 years. The nostrils become packed with dense growth, but there is little constitutional reaction. The disease is the direct cause of death only when it extends into the trachea, bronchi, and lungs and produces stenosis. Cunning and Guerry published a comparatively recent and comprehensive review of the subject.

Pathologically, the disease is a granulomatous inflammation associated with marked fibrosis. The epithelium may be hyperplastic or atrophic. The infiltrate in the stroma is composed of small mononuclear cells in which plasma cells predominate, and there are usually numerous Russell bodies. The latter are not specific for rhinoscleroma but are found in any inflammation in which plasma cells are a prominent element. They are described and illustrated in the section on inflammation. Occasionally the picture is so dominated by the plasma cells that the lesion can be mistaken for plasmacytoma.

The specific feature in the histologic picture is the Mikulicz cell. This is a vacuolated macrophage with a relatively small concentrated nucleus, centrally placed. The vacuoles in the cytoplasm are not fat. The bacteria are demonstrated by silver impregnation and are found in the Mikulicz cells, usually at the periphery. Mikulicz cells are present in varying numbers and distribution, being usually more abundant near the surface. They may be so few and so scattered that they are difficult to identify, and the diagnosis can only be presumptive on the basis of history, intensity of cellular exudate, and amount of fibrosis. The cartilaginous consistency of the lesions is the result of fibrosis, particularly of the older portions, where the bands of collagenous connective tissue that develop often obliterate the more active cellular feature.

It has been recently reported that streptomycin is effective in curing the disease. Irradiation therapy is also helpful.

Syphilis.—The primary lesion rarely occurs in the nose and then usually at the mucocutaneous junction. An early manifestation is enlargement of the preauricular lymph nodes. Secondary lesions are more common, appearing as mucous patches. A less defined and less easily recognized involvement is syphilitic rhinitis. This also produces superficial ulcerations that are resistant to local treatment. The condition may remain undiagnosed until the secondary skin manifestations establish the diagnosis. A refractory superficial ulcerative rhinitis, therefore, should excite the suspicion of secondary syphilis. In the early stages the reaction may be limited to nonspecific erythema of the mucosa.

Among the commonest sites for the tertiary gummatous lesion are the bony nasal septum and the hard palate, although any part of the upper respiratory tract may be involved. The gummatous process invades all structures, bone, cartilage, and soft tissue. The destruction of the bone and cartilage produces the characteristic saddle-back deformity of the nose. Syphilis is the most frequent cause of this deformity, and in the days before treatment with arsenicals and antibiotics it was also the commonest cause of perforation of the nasal septum. Syphilitic condylomas may develop in the nasal cavities.

In CONGENITAL SYPHILIS the flat bones of the skull, including the vomer, may be destroyed, and this increases the incidence of saddle-back nose. One of the most constant symptoms of congenital syphilis in babies is "snuffles" resulting from the chronic coryza. The mucous membrane is swollen, red, and diffusely infiltrated with lymphocytes, plasma cells, and neutrophils in proportion to the degree of secondary infection. There may also be ulceration and necrosis of the mucosa, and the necrosis may involve the cartilage and bone not only of the septum but also of the lateral walls of the nose. Perinasal excoriations of the skin are usually present.

Tuberculosis and **sarcoid** of the nose and paranasal sinuses are discussed in the chapter on granulomatous inflammations (page ....). There are illustrations of the lesions, however, in the plates following this chapter.

Rhinosporidiosis.—This condition was first described by Seeber of Argentina in 1895, but it is endemic in India and Ceylon and several cases have been reported as originating in the United States (Pasternack and Alexander). There are eight cases in the Registry from this country. The causative organism was originally considered to be a protozoon, but in 1922 Ashworth proved it to be a fungus and it has since been known as *Rhinosporidium seeberi.* Dr. Reddy of Madras, India, confirmed the following clinical points during a recent personal interview. All attempts to cultivate the organism and to induce infection artificially in man and animals have been unsuccessful. The method of transmission of the fungus is not known, except that in India where the disease is so common, the infection is apparently acquired in the bathing pools. It occurs almost exclusively in men in spite of the fact that women use the pools with them. The nasal mucosa is the predominant site of infection, but the conjunctiva is occasionally involved, and less frequently, the ear, pharynx, larynx and genitalia.

The infection usually manifests itself as a single polyp attached to the mucosa of the cartilaginous septum. It is red and pebbled like a raspberry. Less commonly there are two or more polyps, and they may be deeper in the nares and hang down in the pharynx. Those that are so located tend to resemble clinically the common nasal polyp.

There is nothing specific in the microscopic picture except the striking and characteristic sporangia that are present in great numbers and in all stages of development. The earliest stage is a small round cell, about the size of an erythrocyte, with a sharply defined membrane. It increases in size and in number of spores until it becomes as much as 150 microns in diameter, having a thin wall and containing approximately 15,000 spores. The oldest spores are in the center and are recognized by their large nucleus and small rim of cytoplasm. The young spores are crowded in the periphery. They are very small and have dark, solid nuclei. A sporangium in the surface epithelium can be seen clinically as a small, yellow projection. On rupture in this position, spores are liberated over the surface of the mucosa, but there is no clinical evidence of autoinoculation. The fungus does not invade or gain access to the internal organs as do many of the other fungi.

When sporangia rupture in the tissues, there is a local intensified inflammatory reaction, and later the remaining chitinous wall gives rise to a foreign-body granuloma. Older portions of the polyp show varying amounts of fibrosis.

The polyps in the anterior portion of the nose are covered by squamous epithelium which may show pseudoepitheliomatous hyperplasia. The bulk of the lesion is made up of vascular, myxomatous, or fibrous connective tissue in which, in addition to the sporangia and foreign body tubercles, there may be small abscesses.

Recurrence is common after removal of the polyps and even after cauterization of the base. Wide and deep tissue removal is necessary to eliminate the spores.

Additional specific inflammations shown in the illustrations are unusual for the nose but have been discussed elsewhere. These include Boeck's sarcoid, a rare infection of mucormycosis, and a foreign body granuloma developing about oil from nose drops. Havens has made a convenient resumé of the granulomatous lesions of the nasal and oral cavities that includes the clinical aspects and suggestions for treatment.

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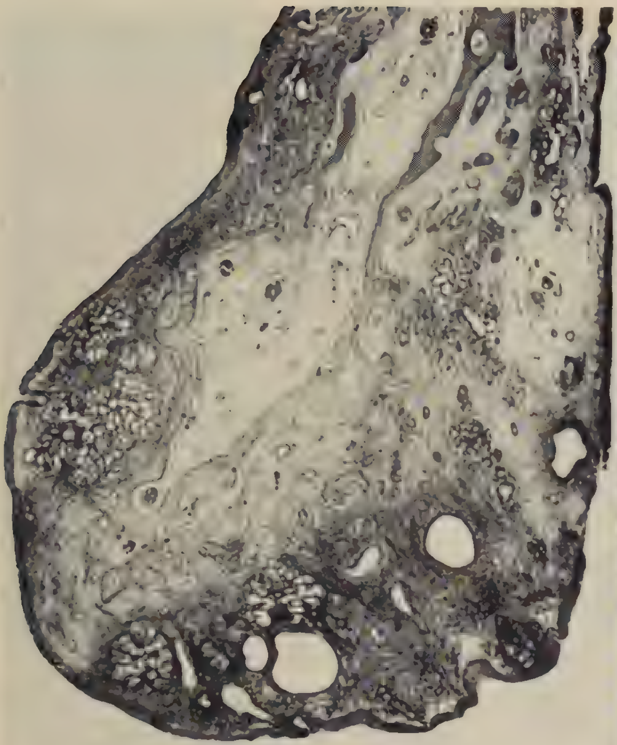
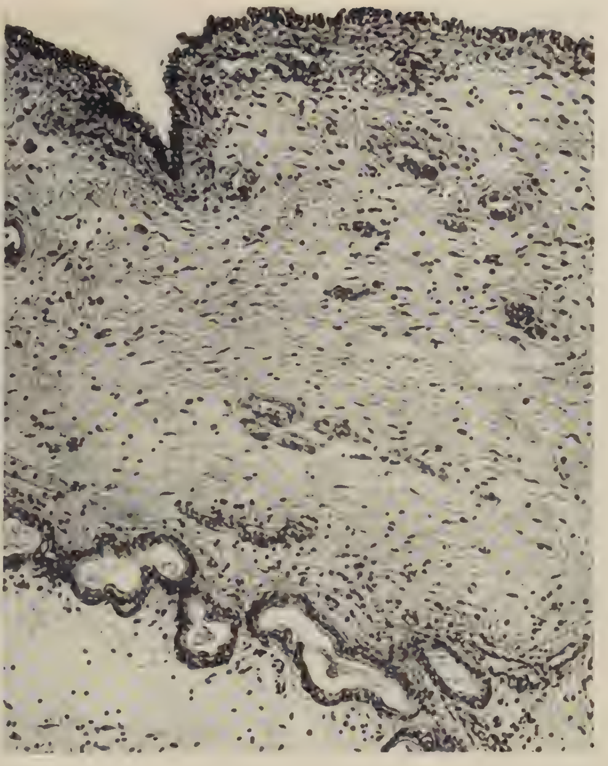
ATROPHIC RHINITIS (OZENA)

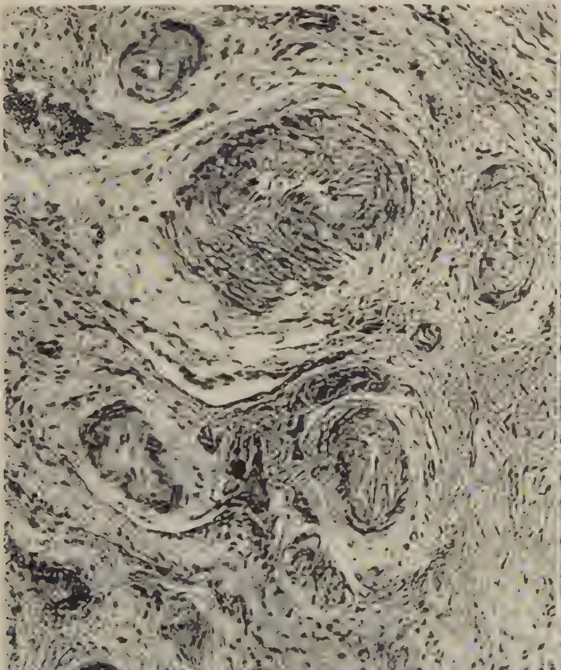
(SCLEROSING RHINITIS–RHINITIS SICCA)



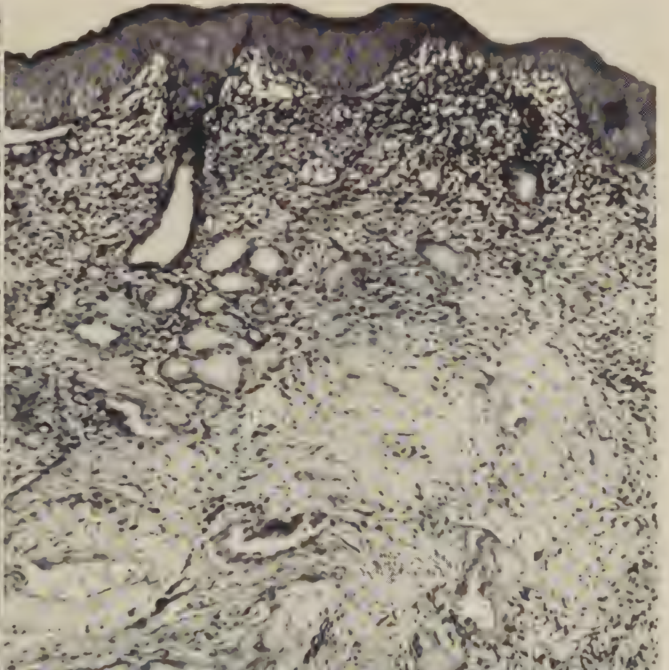
Middle turbinate, showing squamous metaplasia of epithelium; atrophy and fibrosis of stroma; atrophic and a few cystic glands; cavernous plexus reduced in size. (Semenov).



Mucosa of turbinate from another case: epithelium atrophic and altered in type; stroma fibrotic; glands reduced in number. (Ruskin).

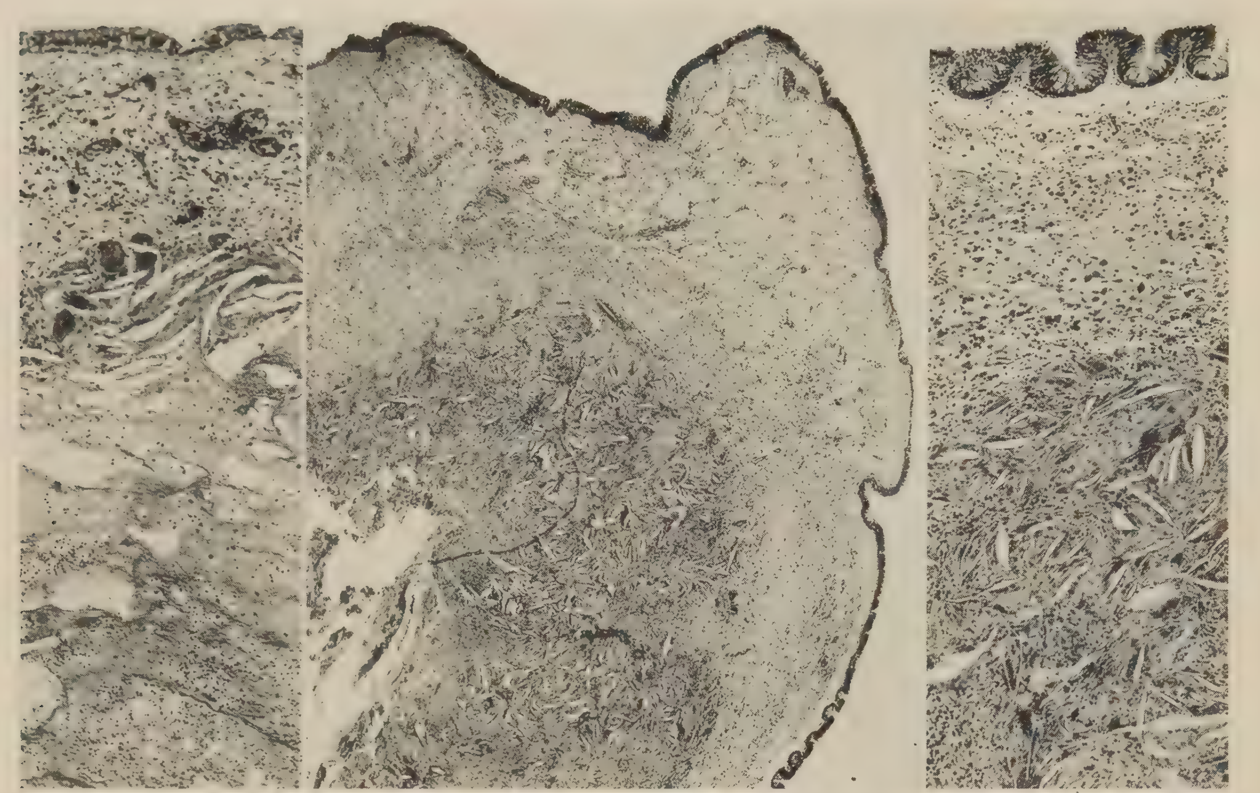


Turbinal mucosa, deep portion, showing marked hyperplasia of media of vessels and fibrosis of stroma. (Ruskin).

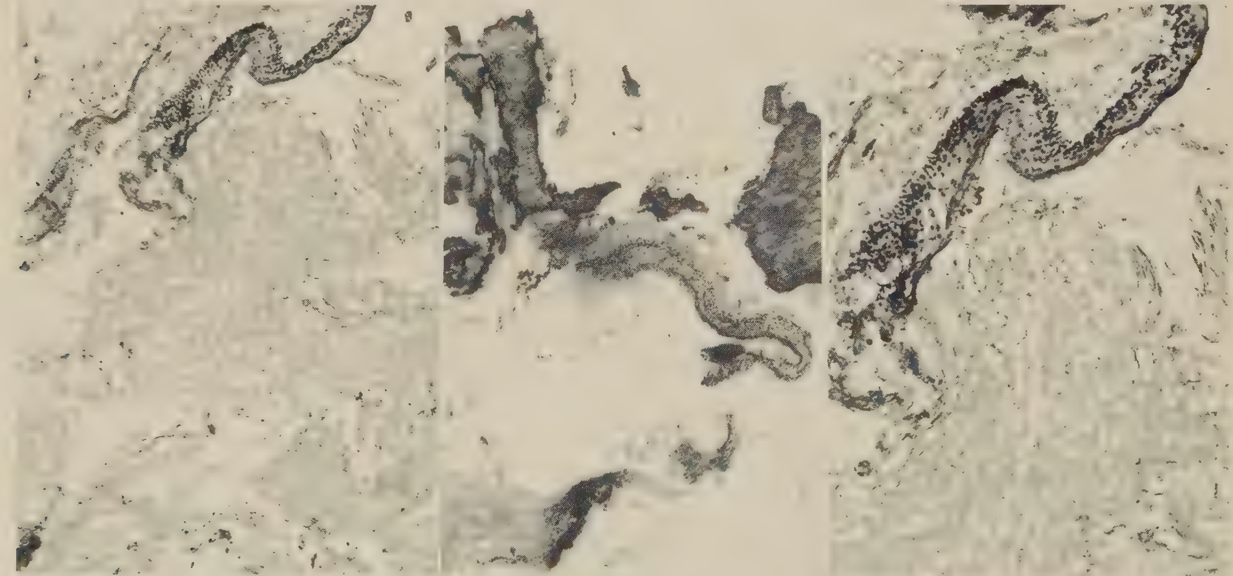


Turbinal mucosa, showing squamous metaplasia of epithelium; atrophic glands; thick vessel walls; fibrosis of stroma. (Semenov).

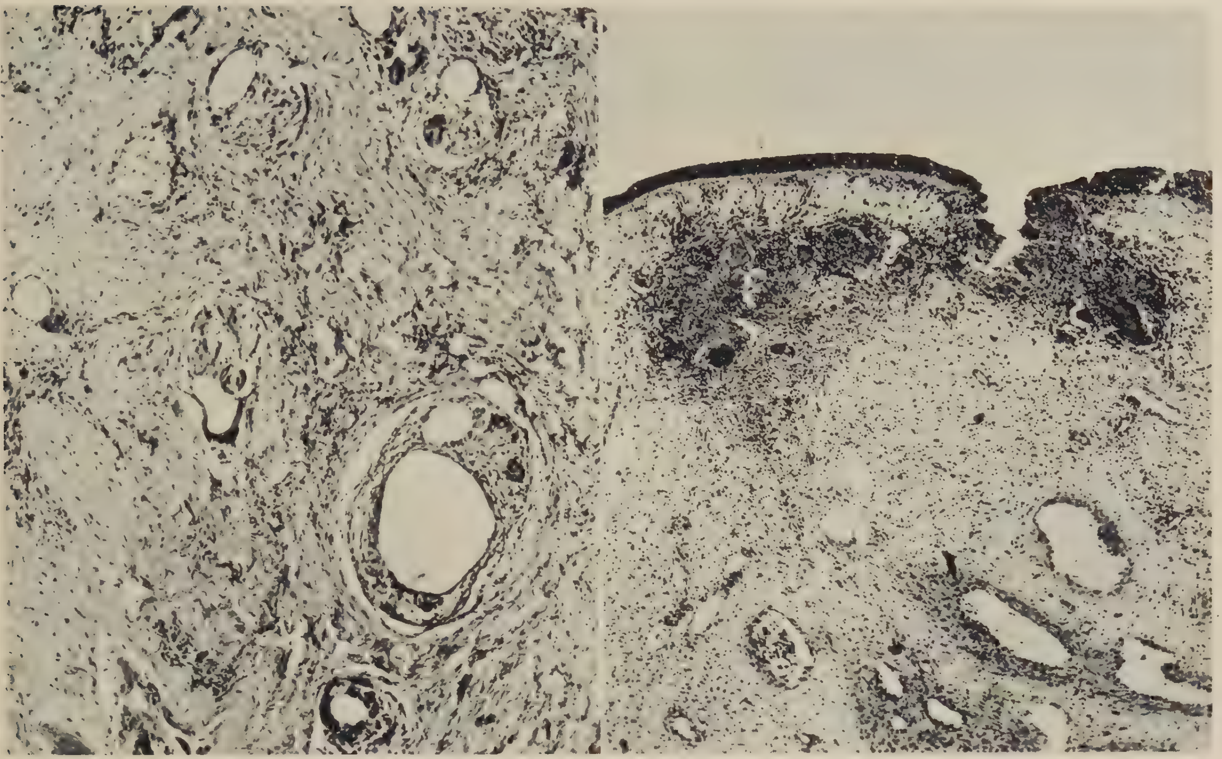
RHINITIS CASEOSA PSEUDO-CHOLESTEATOMA, ANTRUM CHOLESTEATOMA, SINUS



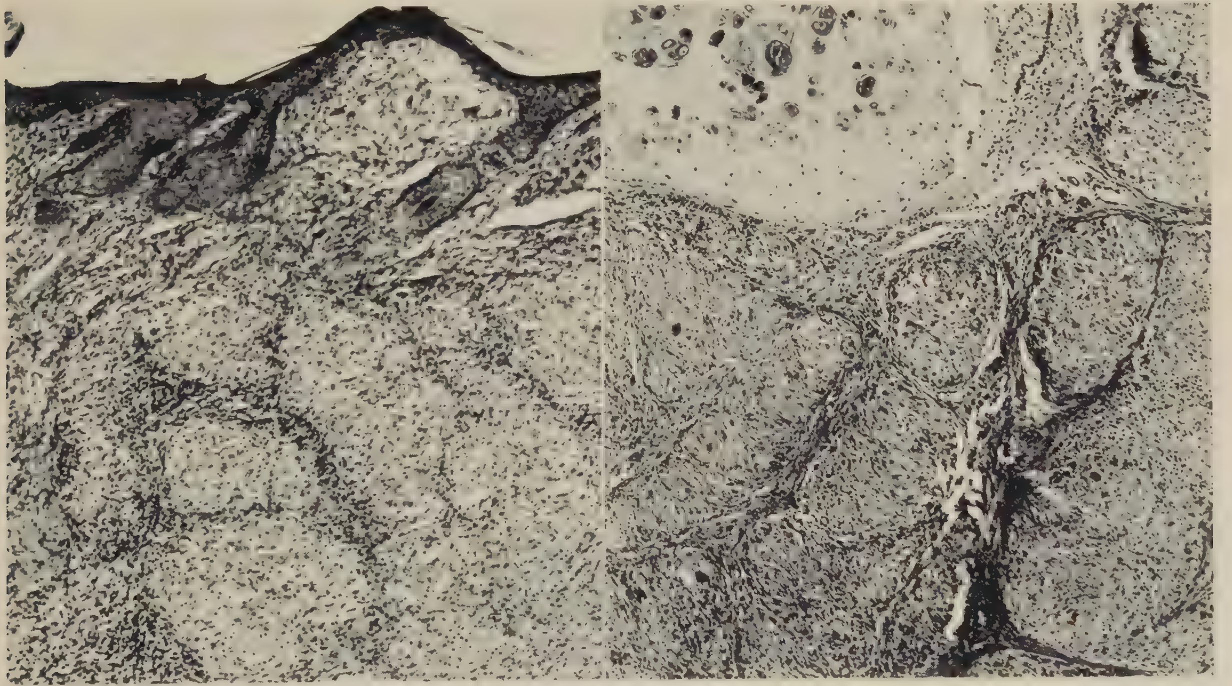
Rhinitis caseosa pseudo-cholesteatoma. Material from maxillary sinus, left, shows many cholesterol slits in foreign body giant cells. x 76. Antral mucosa, from a 22 year old man with progressive pain in upper jaw for 3 years (center and right). At operation, the mucosa, except the posterior portion, was greatly thickened and polypoid. Superficial edema and abundant cholesterol in deeper stroma may have resulted from hemorrhage. The epithelium is intact. x 27 and x 83.



Cholesteatoma, frontal sinus. Keratin flakes and fragments of necrotic bone were removed from frontal sinus of a young man. Pain, gradual bulging of the frontal sinus, and depression of the left eye for some months had given the clinical impression of malignant tumor. The fragment of squamous epithelium seen in picture at left is the clue. x 62, x 62, x 90.

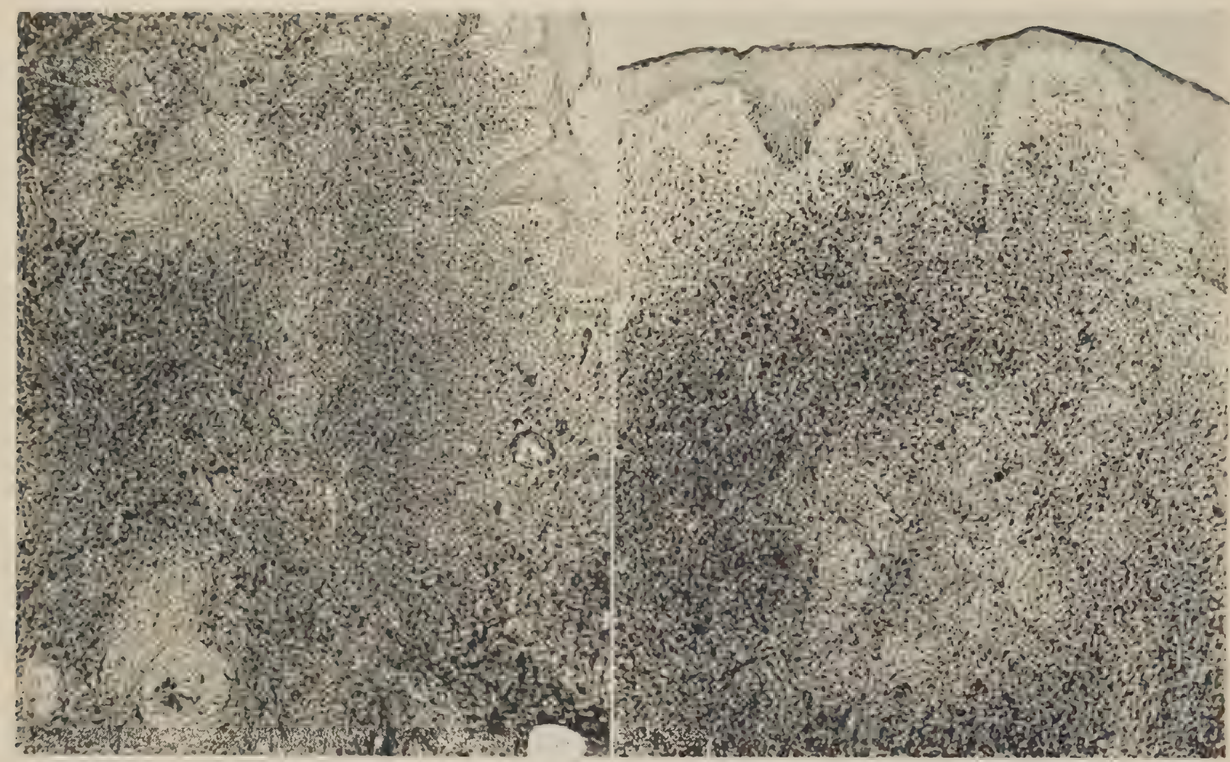


Foreign body granulomas about small and large droplets of oil (presumably injected), chronic inflammatory exudate and dense fibrosis of surrounding nasal mucosa. Histologic features typical of the once common paraffinoma. *Left,* x 75. *Right,* Foreign body reaction in superficial ethmoid mucosa to unidentified particulate matter. Numerous giant cells and polymorphonuclear leukocytes as well as mononuclear cells. x 55.

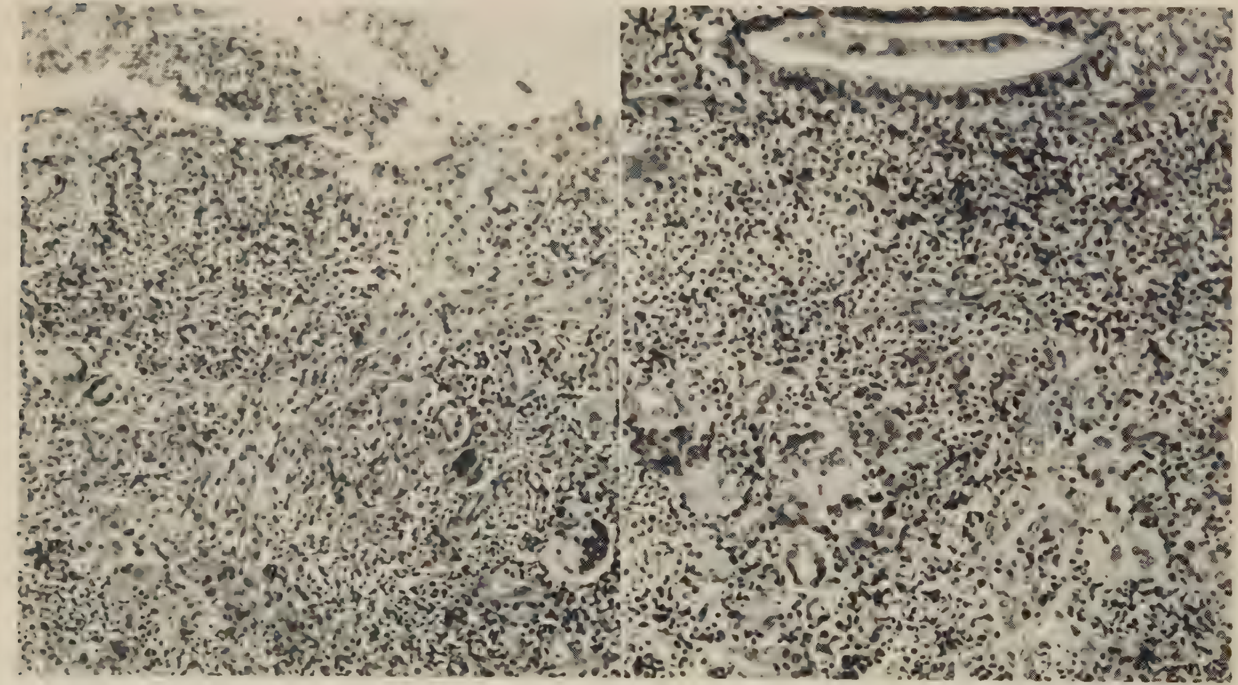


Sarcoidosis. Non-caseating tubercles, discrete and confluent, composed of epithelioid cells and occasional giant cells of Langhans and foreign body type. Scanty or absent peripheral zones of lymphocytes. Extensive involvement of nasal mucous membrane with granulomas extending to squamous epithelium of vestibue (*left,* x 88) and to the perichondrium of the cartilaginous septum, in another case (*right,* x 76).

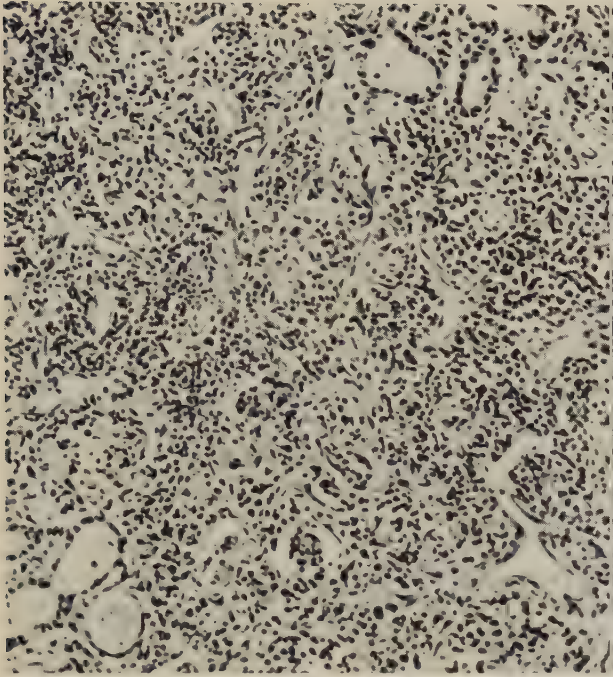
TUBERCULOSIS



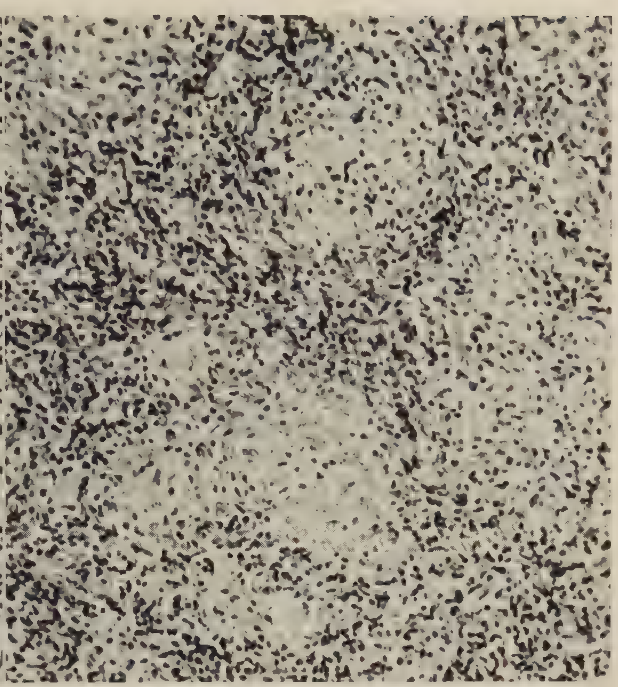
Tuberculosis of the upper respiratory tract is usually secondary, as in this case, to pulmonary tuberculosis, although cases of primary infection of the nasal cavity, tonsils and larynx are reported. Normal structure of the greatly thickened turbinal mucous membrane is obscured by discrete and conglomerate tubercles surrounded by massive accumulations of lymphocytes. Squamous metaplasia of surface epithelium. x 48, x 62.



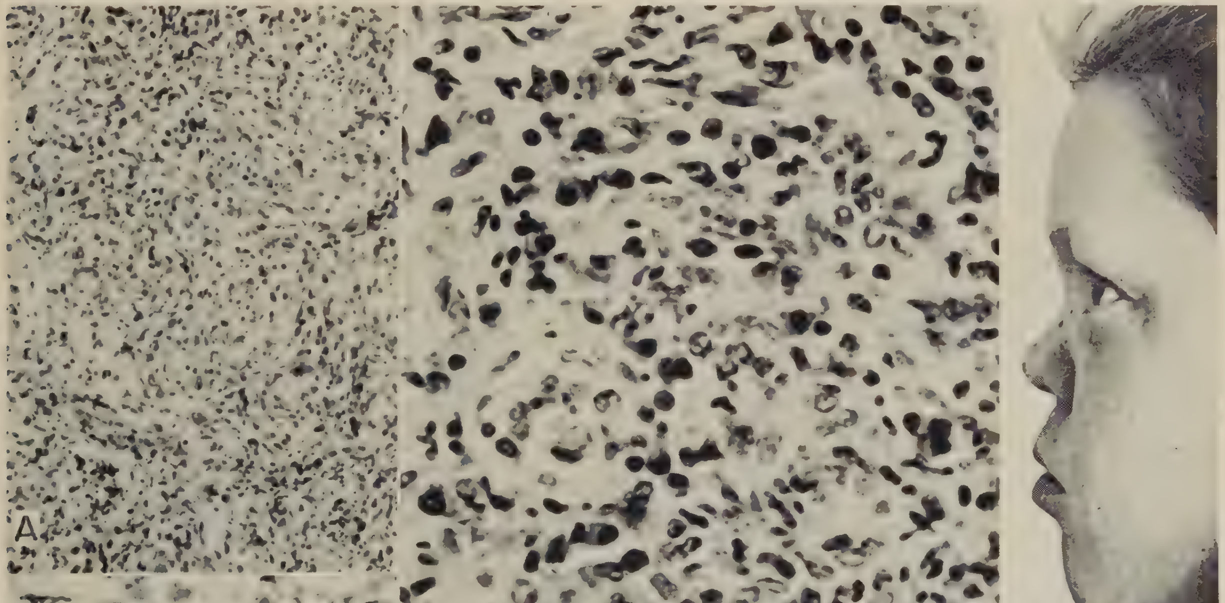
Granulomatous inflammation with suppuration, secondary to surface ulceration, nasal cavity. Numerous giant cells of both Langhans and osteoclastic type. Extensive polymorphonuclear infiltration at surface *(left)* and deep within lesion *(right)*. This nasal biopsy originally diagnosed syphilis and giant cell tumor; the patient died of pulmonary tuberculosis. x 125, x 165.



Syphilitic rhinitis. Septal mucosa from a young colored woman with secondary lesions and serologic evidence of lues; stroma greatly thickened by fibrosis and infiltration by plasma cells and lymphocytes.

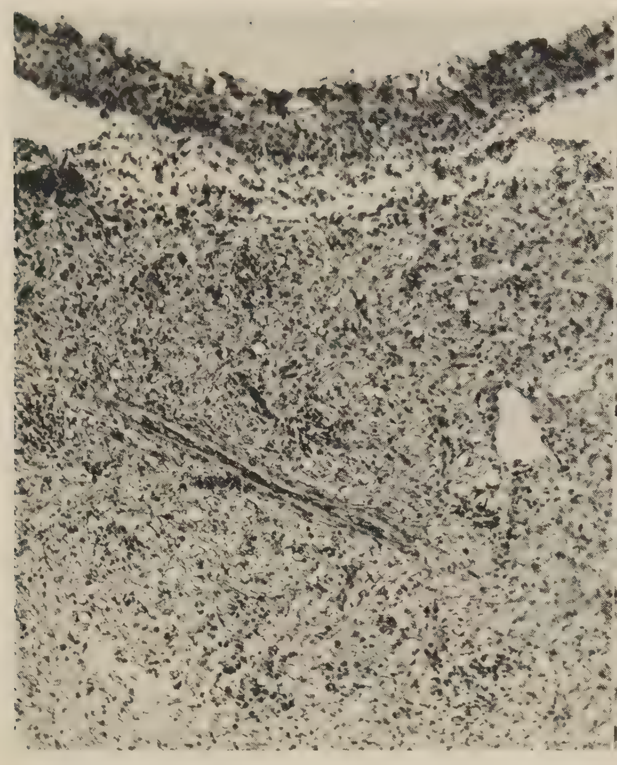


Granulomatous reaction, nasal mucosa of a young colored woman with secondary lesions and serologic evidence of syphilis. Discrete granulomas composed of epithelioid cells within dense mononuclear exudate. x 185.



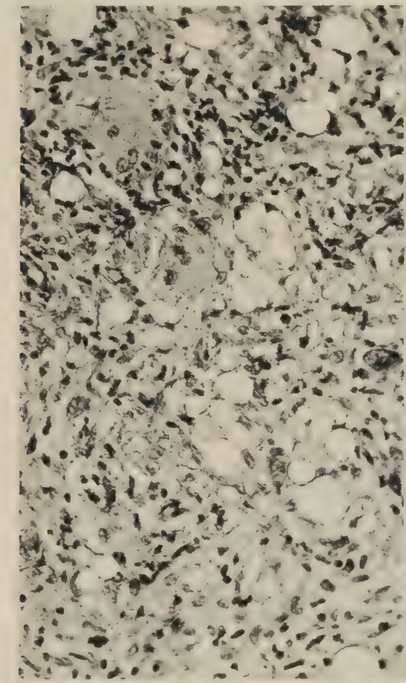
A. Syphilitic granulation tissue (not granulomatous) in nasal mucosa (x 150) swarming with *T. pallidum* (**B,** x 1100). **C.** Endarteritis and the predominantly plasma-cell exudate in same case. x 550. **D.** Saddle nose of congenital syphilis from gummatous destruction of bone.

LEPROMATOUS LEPROSY

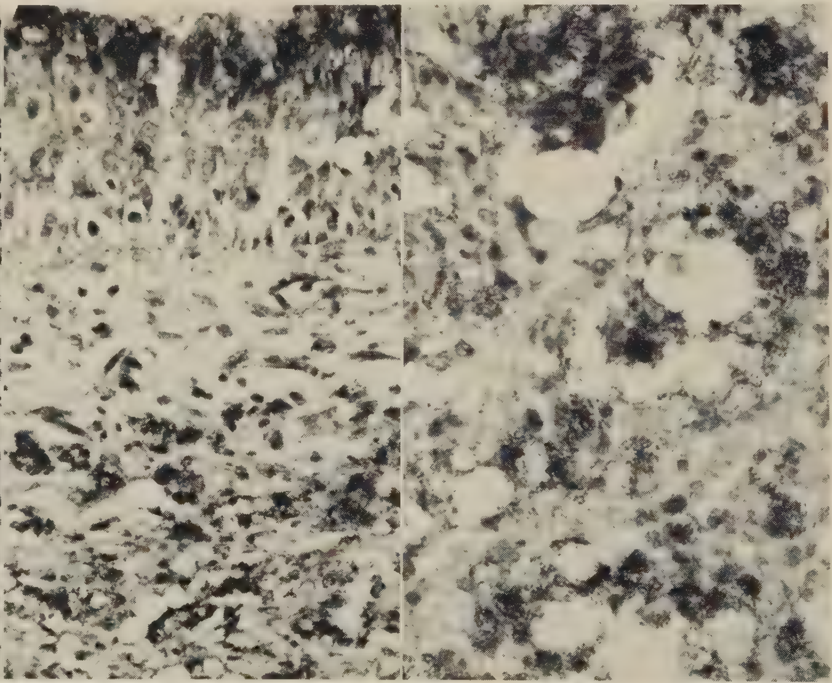


The nasal mucosa may be particularly involved in lepromatous leprosy, which may attack any part of the upper respiratory tract. Diffuse lepromatous infiltration of mucosa of middle turbinate. x 100. (C. Binford, Wash., D.C.)

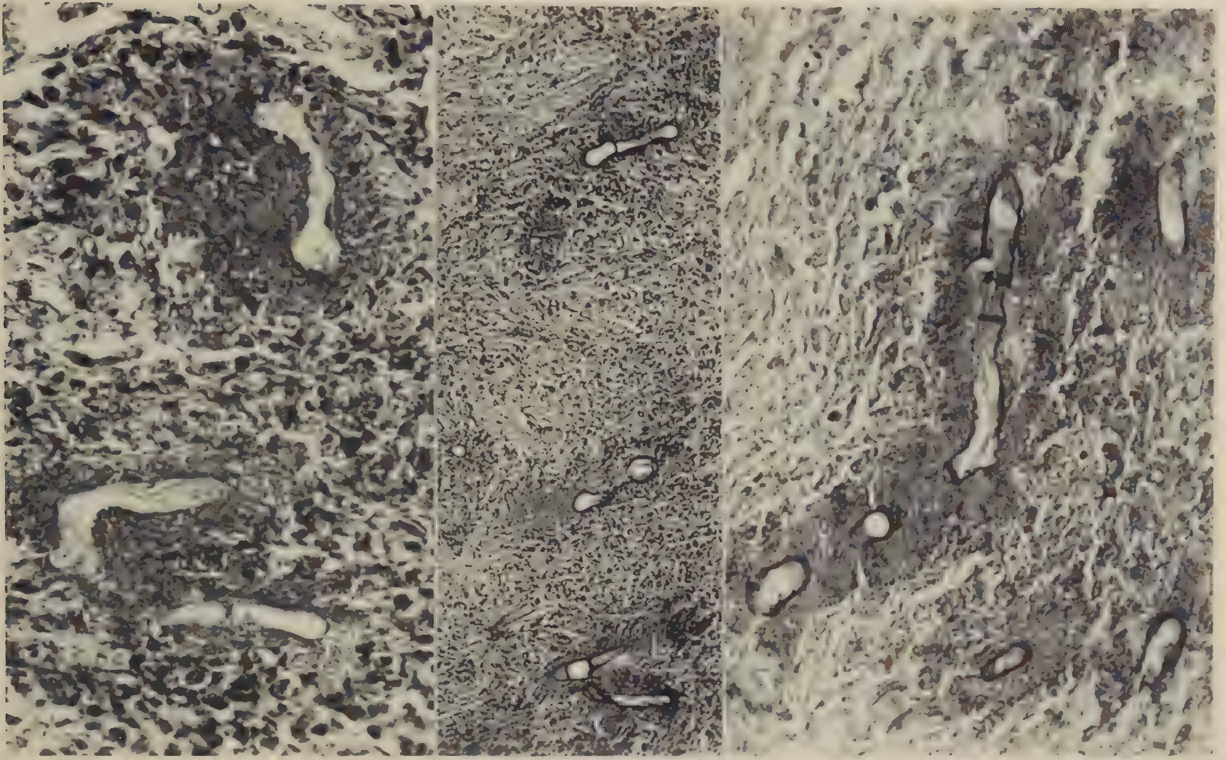
Lepra cells. Dense accumulations of foamy and vacuolated histocytes in nodular granulomatous lesion of middle turbinate, biopsied because malignant tumor was suspected. Normal glandular structures have disappeared. x 625.



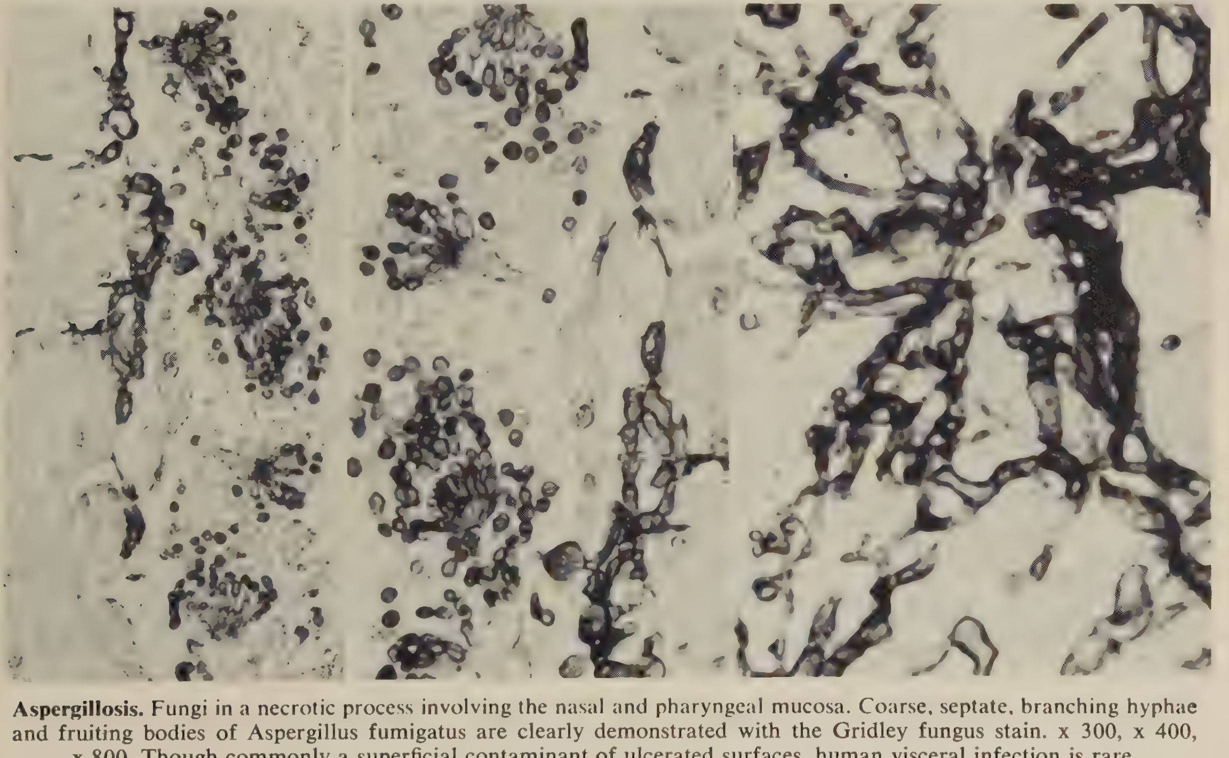
Giant cells, frequently vacuolated, may be present. Several in this field, upper one with asteroid. x 210.



Mycobacterium leprae are demonstrated by acid-fast stains, in massive numbers within lepra cells. Positive diagnostic nasal smear could probably have been obtained because of the numerous organisms within the epithelium. Compact masses of bacilli produce the globi and rosette formations. x 275, x 660.



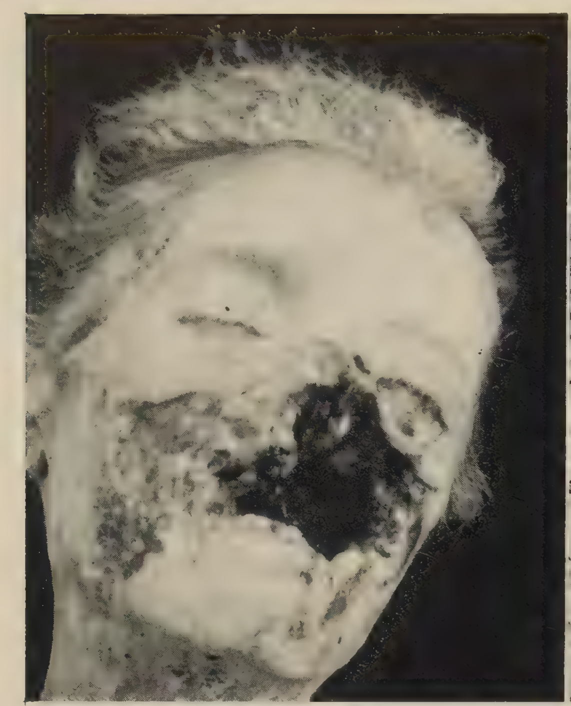
Mucormycosis. Intranasal and subcutaneous swelling, in a 17 year old male, was originally diagnosed malignant tumor; later, coccidioidomycosis. The extremely broad nonsegmented hyphae have stimulated an intense granulomatous inflammation. The discrete granulomas have strikingly eosinophilic, granular central areas. x 395; Bauer stain, x 145 and x 395. Unusual case because it was not fatal; occurred in a patient who was not diabetic; stimulated a granulomatous rather than a suppurative reaction. Paranasal sinuses and orbit have been considered the usual pathway of infection.



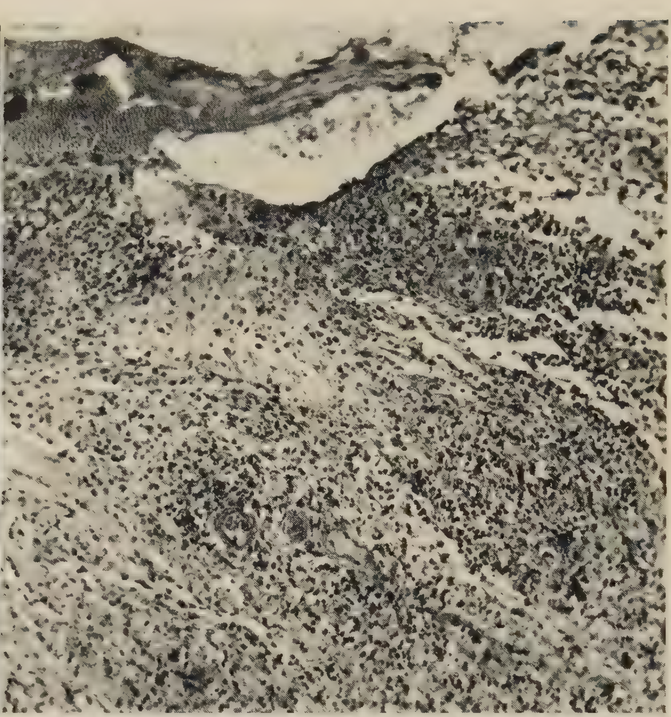
Aspergillosis. Fungi in a necrotic process involving the nasal and pharyngeal mucosa. Coarse, septate, branching hyphae and fruiting bodies of Aspergillus fumigatus are clearly demonstrated with the Gridley fungus stain. x 300, x 400, x 800. Though commonly a superficial contaminant of ulcerated surfaces, human visceral infection is rare.

INFLAMMATION OR NEOPLASIA?

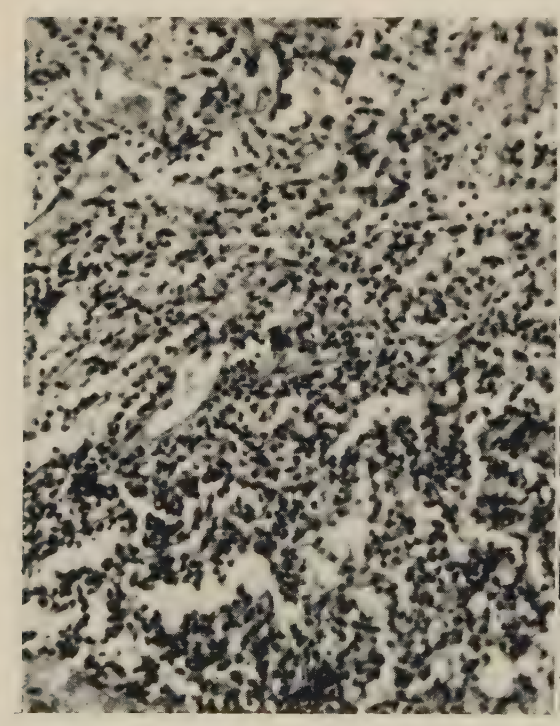
DIAGNOSTIC (BIOPSY) PROBLEMS



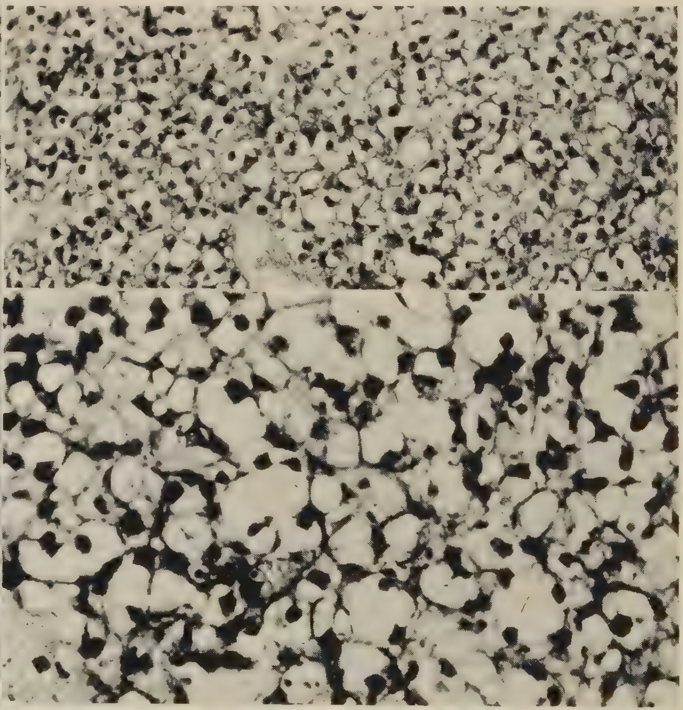
"Idiopathic (lethal) granuloma of midline facial tissues"—a probable case. Progressive destruction of nose, face and pharynx, the pathogenesis of which is not clearly defined. (Göttingen University, Germany, courtesy of W. Putschar, Charleston, W. Va.)



Inflammation versus neoplasia. Idiopathic ulceration with nonspecific exudate. Thoroughly studied but clinically undiagnosed case. x 125. Malignant tumor may remain undiagnosed if only superficial biopsy of secondary ulceration is obtained for histologic study.



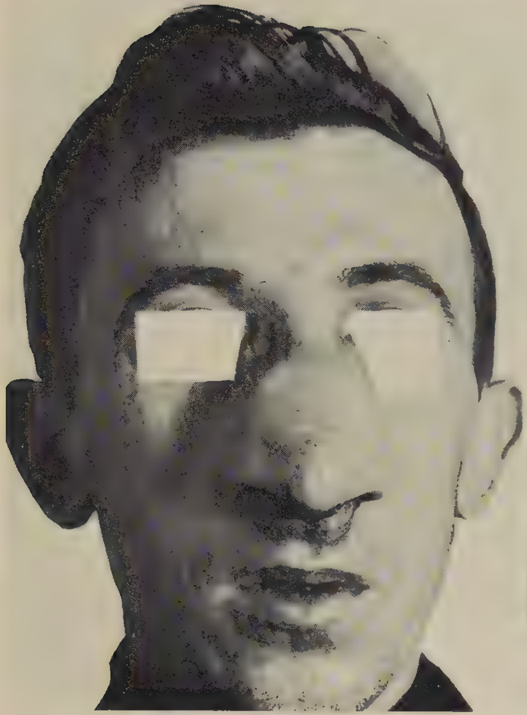
Granuloma or malignant tumor? Progressive fungating lesions of nose and throat with ulceration. Variously diagnosed as infectious graunloma, malignant lymphoma and carcinoma. x 220.



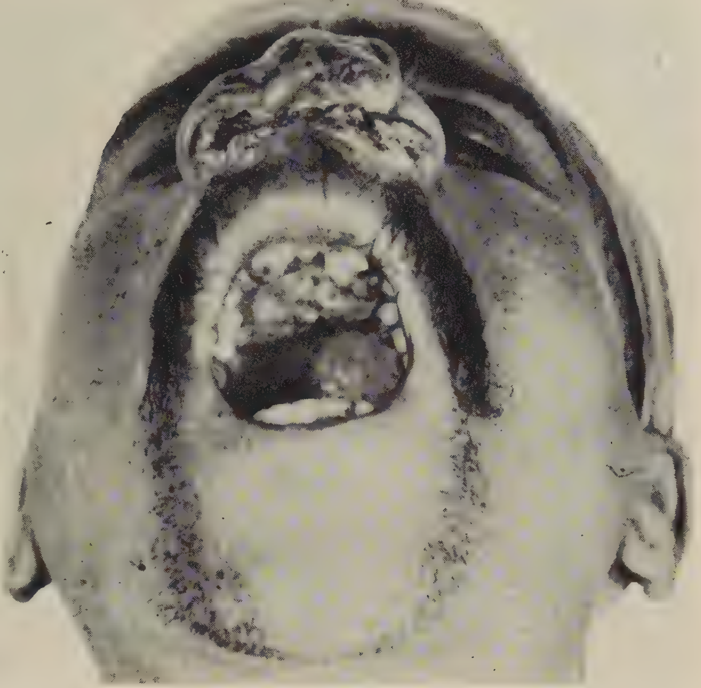
Granulomatous inflammation or neoplasia? Clear cell areas in primary carcinoma of the antrum with extensive nasal involvement, diagnosed and treated as rhinoscleroma. Such cells in biopsy specimens were interpreted as Mikulicz cells. x 185, x 355.

RESPIRATORY TRACT SCLEROMA

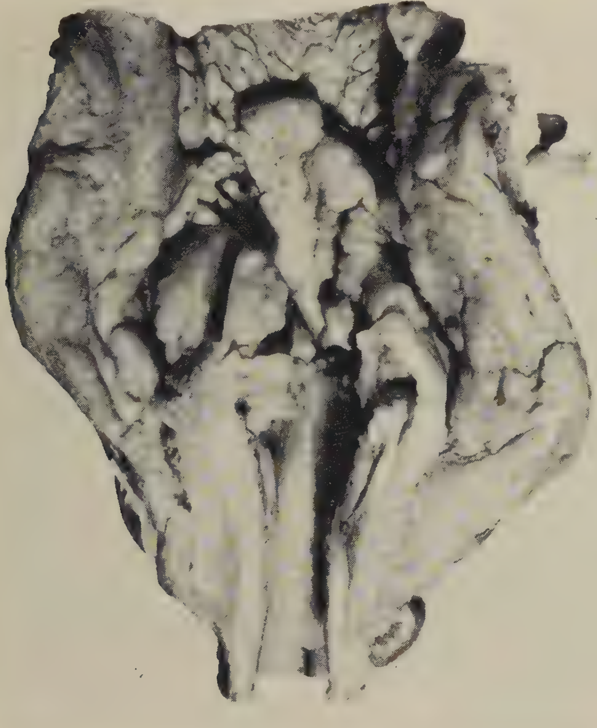
(RHINOSCLEROMA)



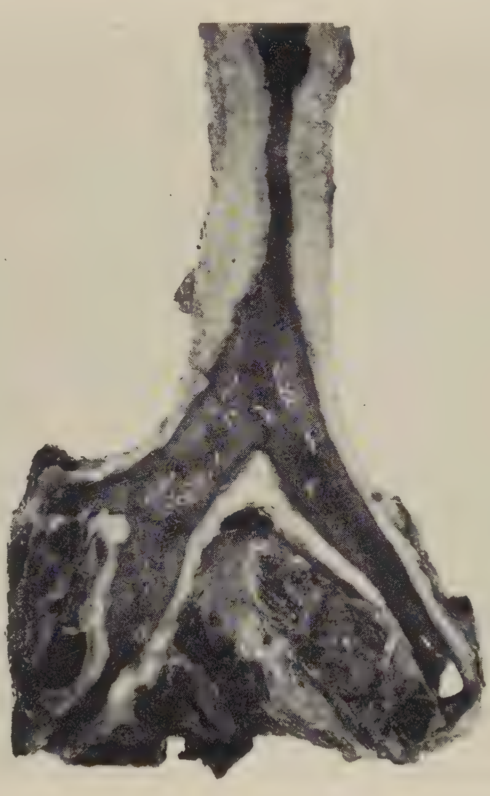
Nose, broadened and deformed by rhinoscleroma of two years' duration, in a 22 year old man. Severe nasal involvement and early extension to tissues of upper lip.



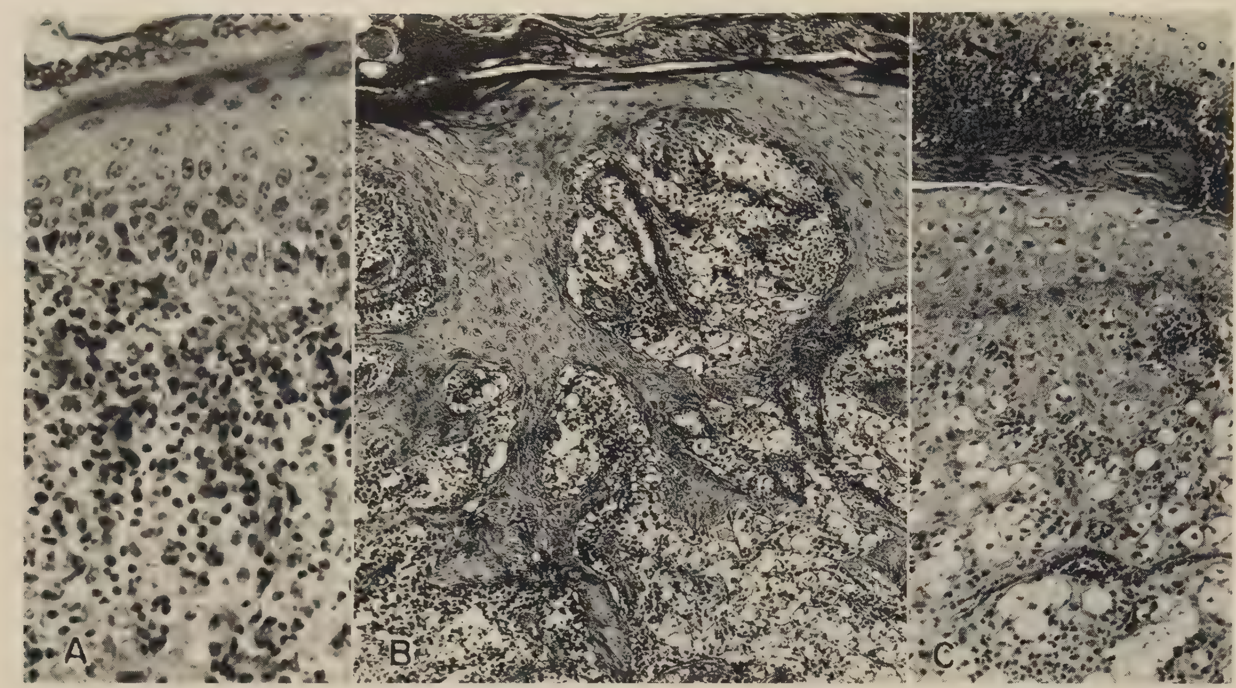
Palate and pharynx, as well as nose, have been extensively involved. The patient is from Egypt, an endemic center. (H. K. Giffin, Omaha, Neb.)



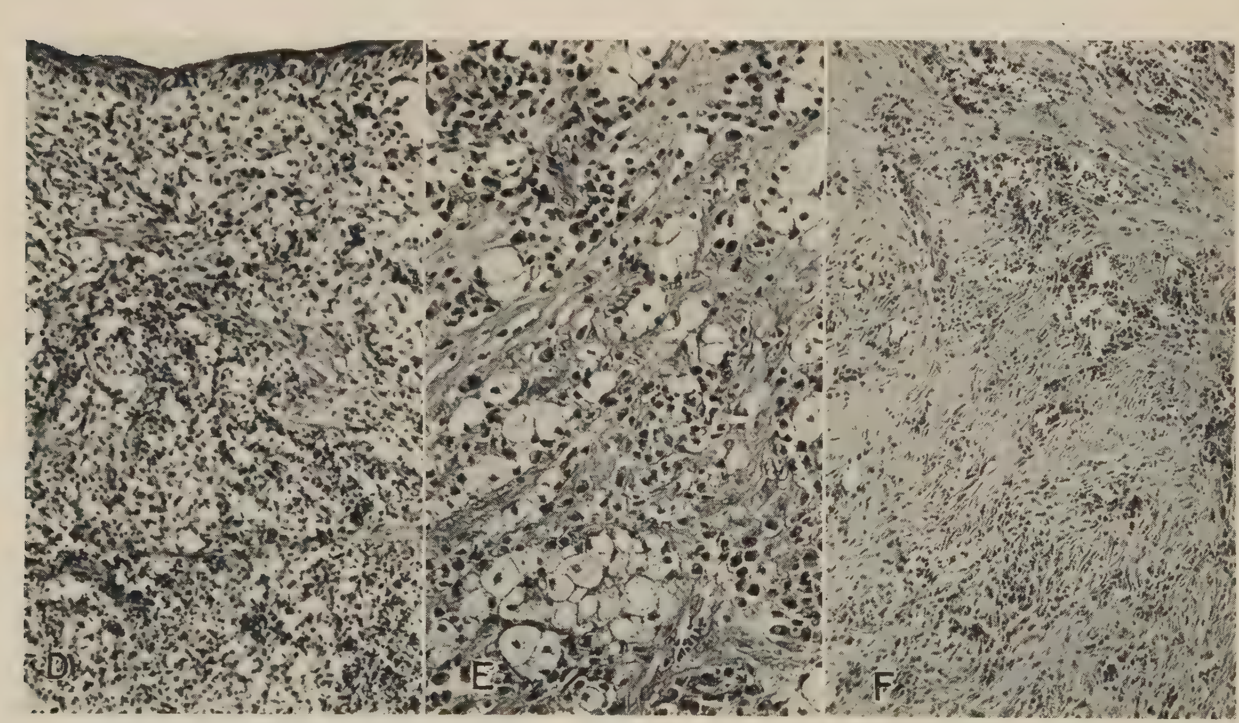
Larynx, from a young Negro man, who had never been out of Washington, D. C., showing dense nodular thickening from scleroma which did not involve the nose.



Trachea and bronchi from another patient are greatly thickened. Extension to lower respiratory tract is not common. (J. McNaught, Denver)



Mikulicz cells, the diagnostic feature: large or small collections of foamy cells, most prominent near the surface (**B** and **C**); sometimes less conspicuous as individual cells, partially obscured by dense plasma cell exudate (**A**) or superficial suppurative exudate (**C** and **D**).

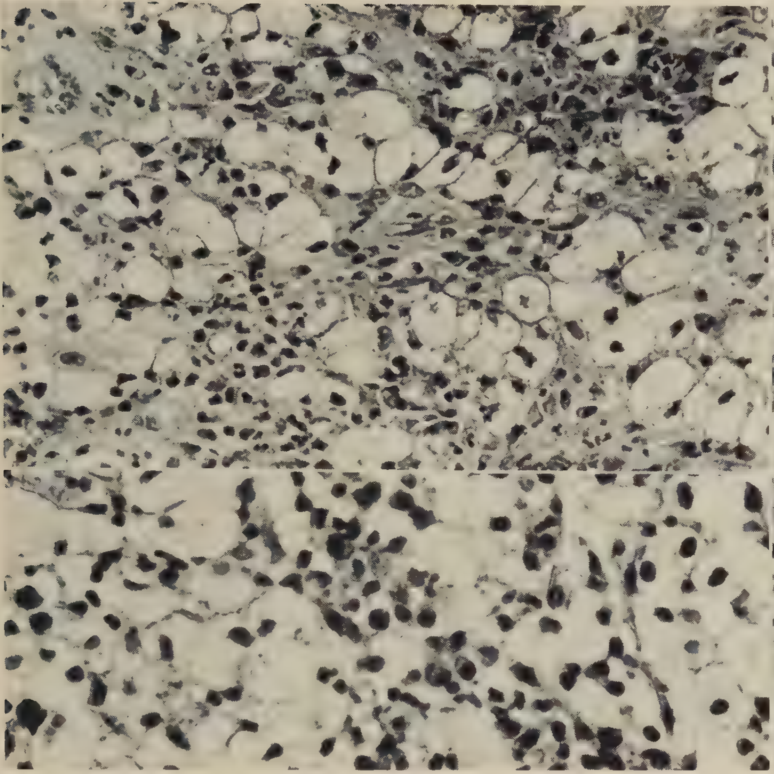


The epithelium may be normal or atrophic (**D**). Usually there is squamous metaplasia with mild or moderate acanthosis (**A**, x 350); pseudoepitheliomatous hyperplasia that may be pronounced (**B**, x 90); or crusted exudate, in presence of secondary infection (**C**, x 145).

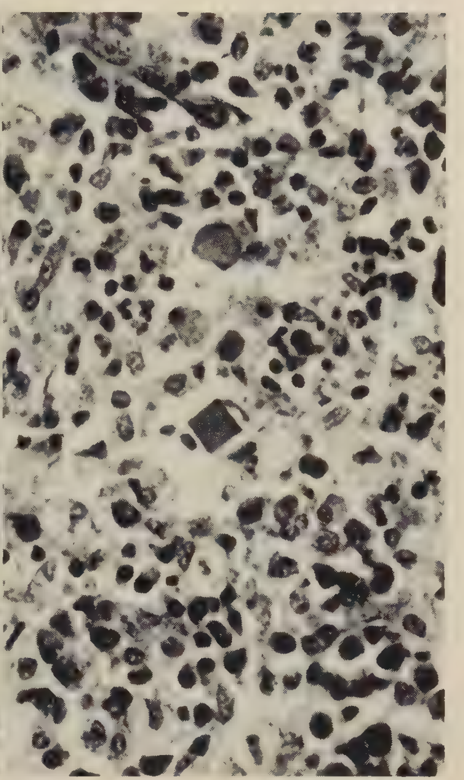
Progressive fibrosis. Delicate strands of fibrous tissue (**D**, x 145) and more advanced fibrosis (**E**, x 205) in surface of active granulomatous lesions composed of Mikulicz cells and plasma cells. **F.** The contracted sclerotic areas for which the disease is named, give the cartilaginous consistency to the lesions and produce the stenosis of the larynx, trachea, and bronchi that may be fatal. x 114.

UPPER RESPIRATORY SCLEROMA

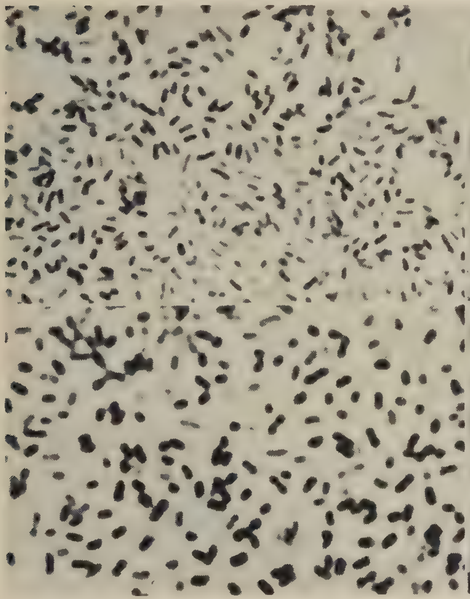
KLEBSIELLA RHINOSCLEROMATIS



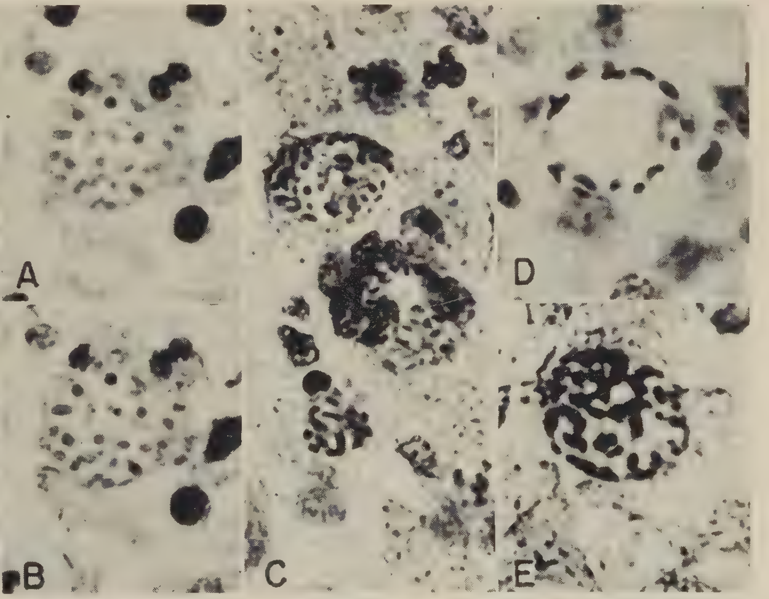
The Mikulicz cells are usually large with foamy, vacuolated or clear cytoplasm and small nuclei. In good routine preparations, faintly stained von Frisch bacilli may be recognized within some cells. x 355, x 435.



Cellular infiltrate consists predominantly of plasma cells, which have produced Russell bodies seen above. Lymphocytes, and occasional polymorphonuclear leukocytes also present. x 500.

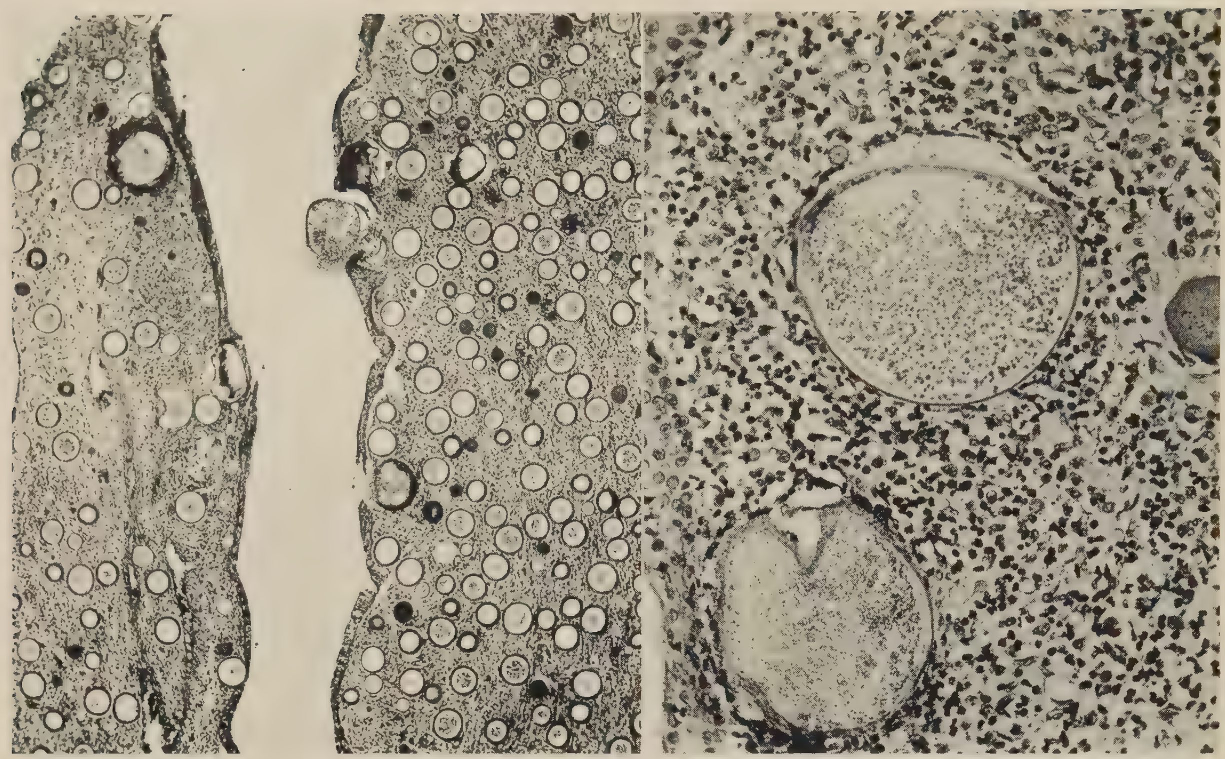


Klebsiella rhinoscleromatis, the possible etiologic agent, is a short, rounded, encapsulated gram-negative bacillus, as seen in these cultures from two Egyptians. x 1800.

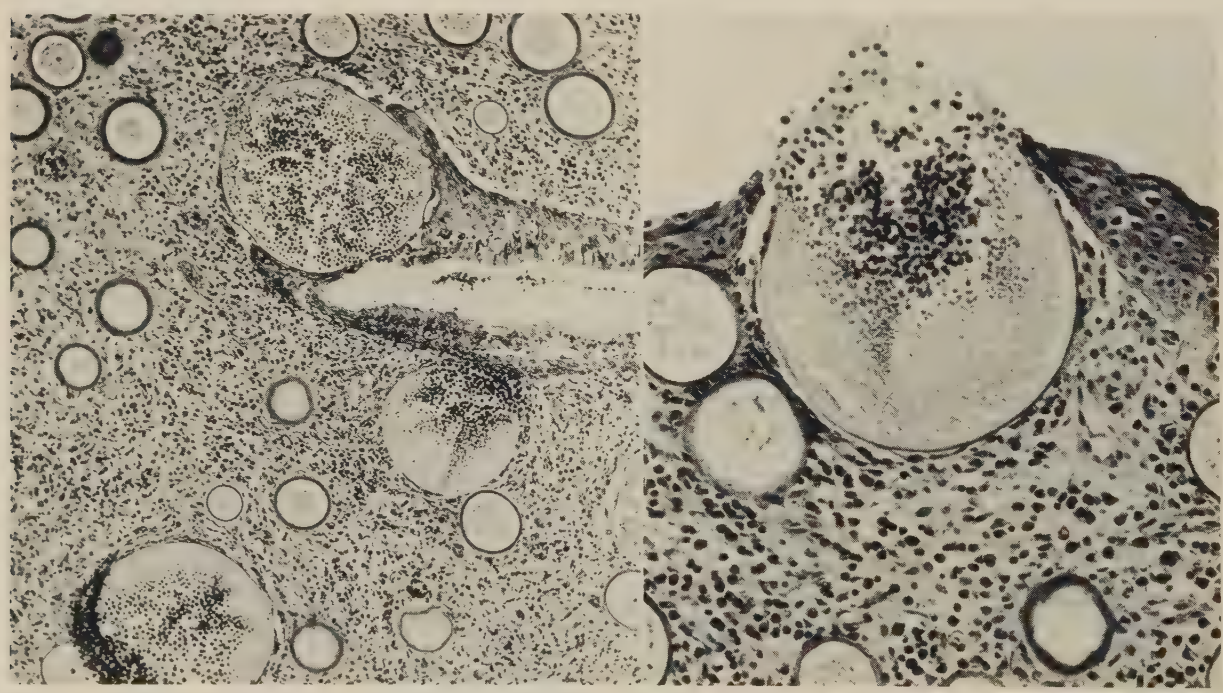


Klebsiella within the Mikulicz cell may be evenly distributed (**A** and **B**), or clumped (**C**) and circled about the periphery (**D**); and are brilliantly stained by various methods. **A.** Hematoxylin and eosin. **B.** Same cell restained–Giemsa. **C.** Warthin-Starry. **D.** Toluidine blue. **E.** Methylene blue. All x 1000, except **E,** x 1500.

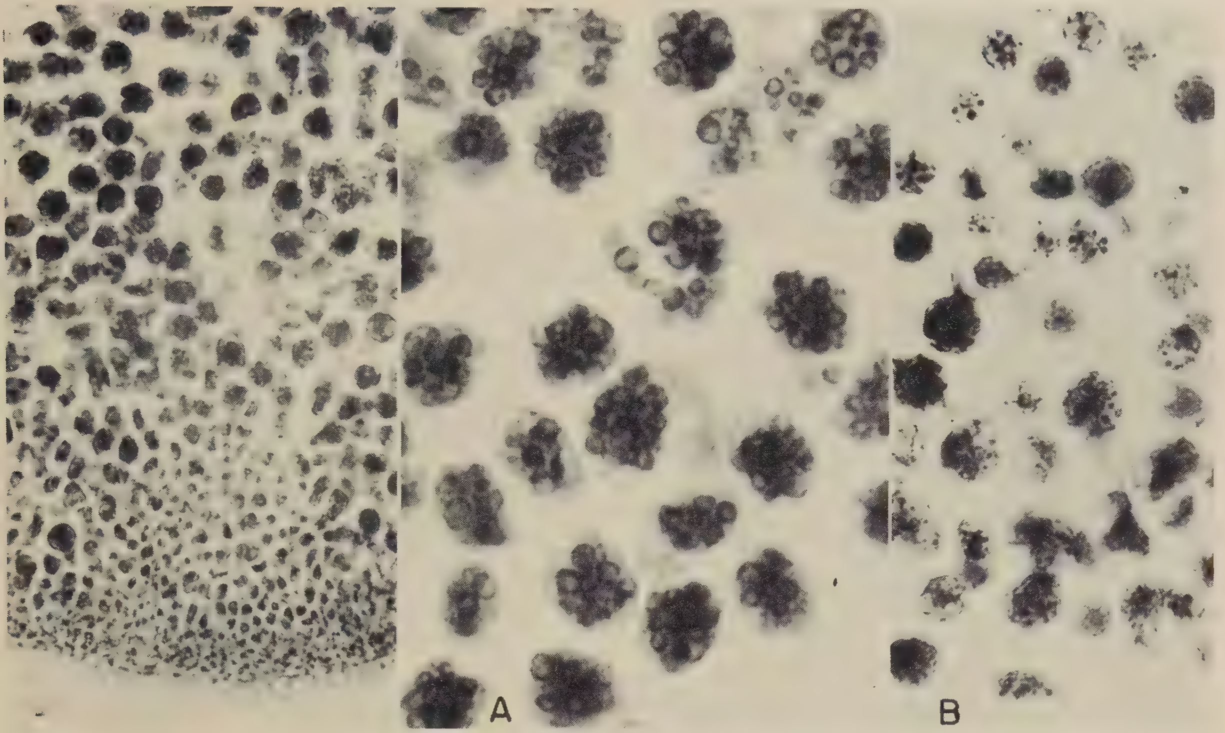
RHINOSPORIDIUM SEEBERI



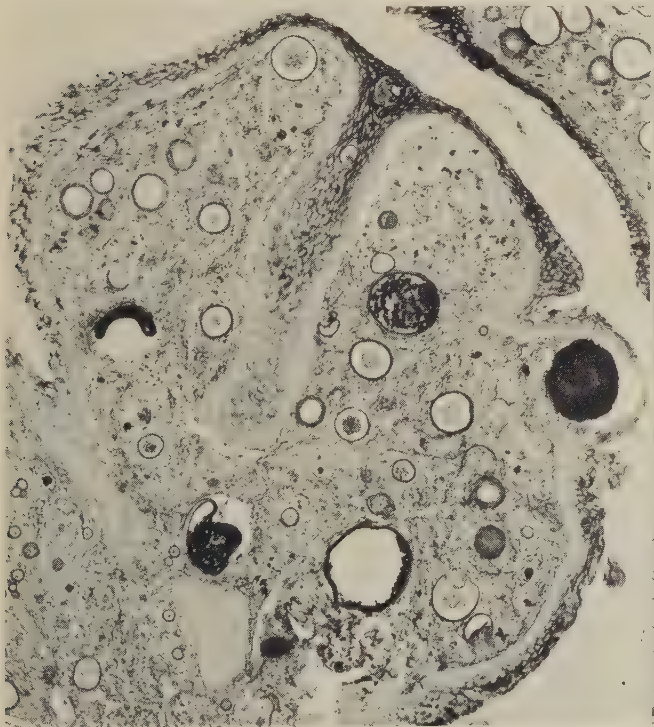
Sessile or pedunculated, persistent, polypoid lesions occur most commonly within the nasal cavity. *Left:* field from a typical nasal "strawberry-like" polyp flecked with grossly visible, pale opaque spots, that are mature sporangia at or near the surface. Developing organisms throughout the mucosa, most in trophic or early nuclear division stages. x 48. *Right:* two organisms, the lower in an advanced stage of nuclear division; the upper in early stage of cytoplasmic division.



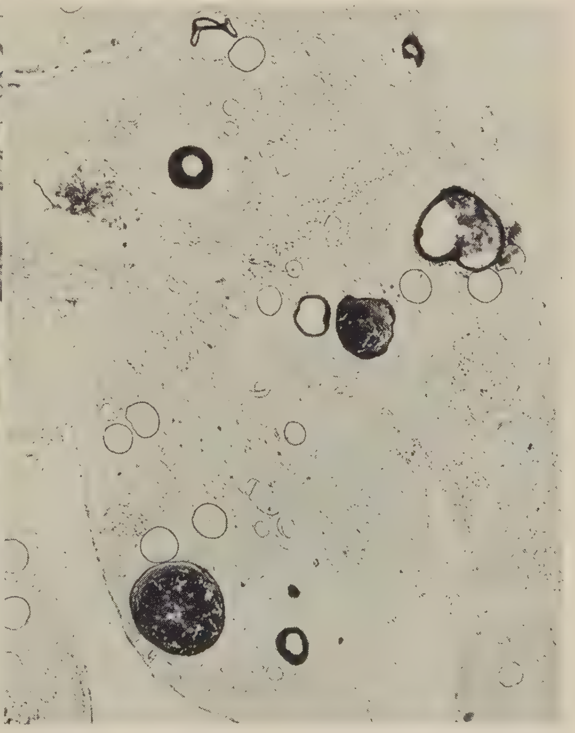
Rhinosporidium seeberi, the etiologic agent, is now believed to be a fungus, but it has never been cultured. When 4000 nuclei are present, division of the cytoplasm occurs around the nuclei, forming the young spores *(upper right). Left:* three mature sporangia, one within epithelium, each contains about 16,000 spores in varying stages of maturation. x 90. *Right:* a mature sporangia discharging its spores through its pore onto the mucosal surface. x 230.



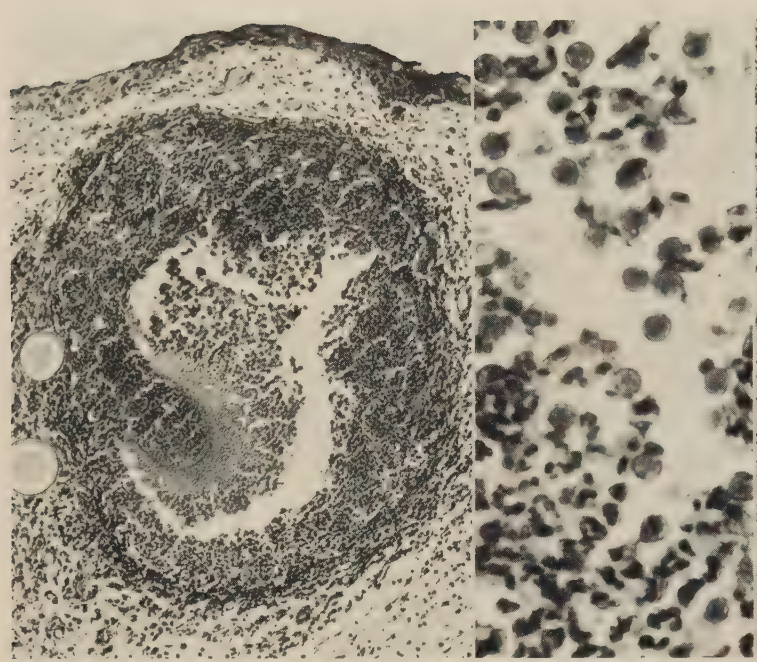
Maturation of spores progresses from the envelope toward the center of the sporangium and toward the incipient "pore." x 600. **A. The mature spore** is a segmented structure, each segment containing a prominent rounded body—the spherule. The spherules are prominent, but the spore capsule can be seen in only some spores. x 1620. (Spore capsules and the "mucilaginous" matrix surrounding the spores are positively stained with mucicarmine.) **B.** Reticulum stains demonstrate a black central area in each segment; it has no known anatomic or physiologic significance. x 865.



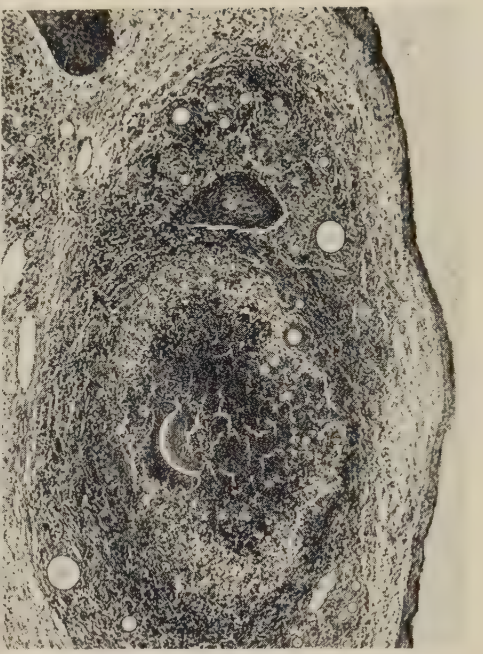
Periodic acid-Schiff reaction: organisms, particularly the mature sporangium and its envelope, are brilliant red. x 90.



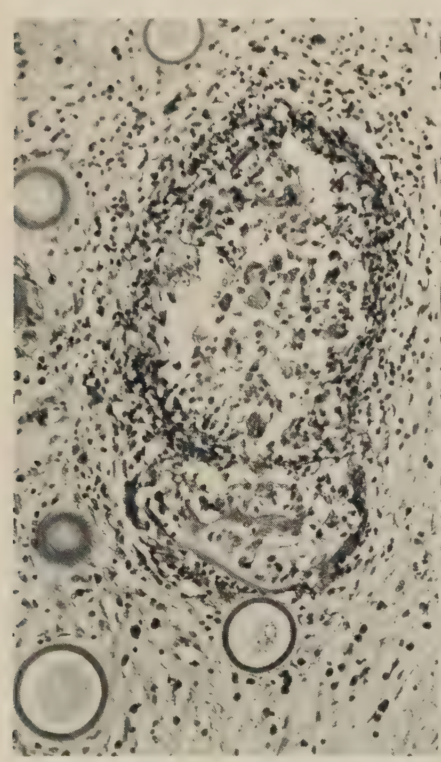
Gridley fungus stain: mature sporangia and empty envelopes are deep violet or reddish purple. Younger forms stain less vividly. x 70.



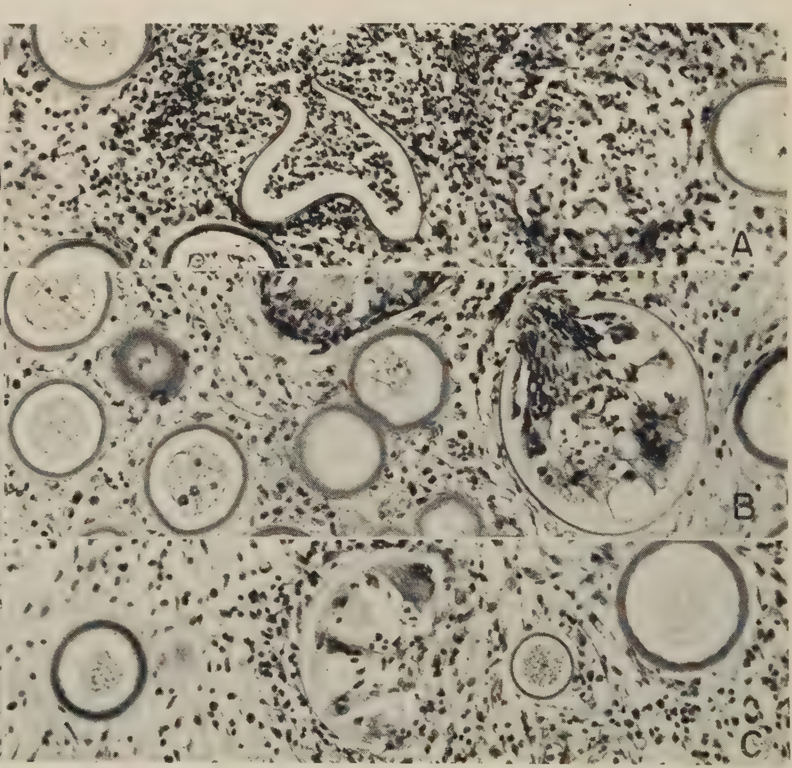
Acute suppurative reaction localized about a recently emptied sporangium. The inverted envelope with adherent young spores and peripheral mature spores lies in the center of the abscess. x 115. Eosinophils and polymorphonuclear leukocytes predominate in the exudate. Spores at top and center. x 545.



A granuloma has developed about emptied sporangium. Remnant of envelope in center surrounded by polymorphonuclear leukocytes and thick peripheral zone of epithelioid cells. x 55.

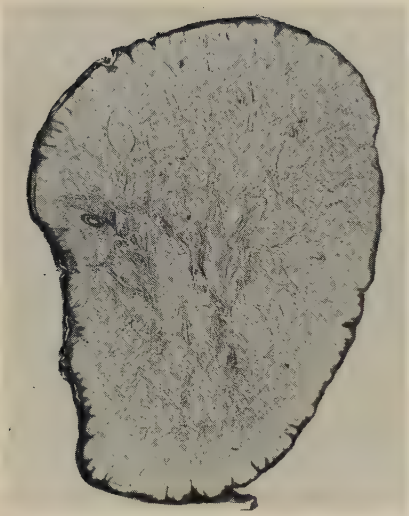


Foreign body granuloma with plasma cell and lymphocytic exudate about a fragment of envelope. Several young organisms in surrounding tissue. x 125.

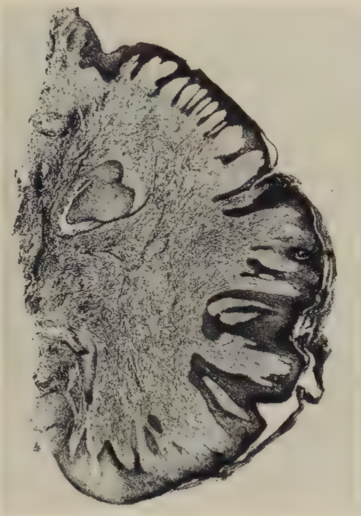


Invasion of emptied envelope through well-defined pore by polymorphonuclear leukocytes and eosinophils (**A,** x 125); fibroblasts and mononuclear cells (**B,** x 145); stromal cells and foreign body giant cells (**C,** x 145). Each figure distinctly shows the two layers (inner cellulose, outer chitinous) of the envelope. x 145.

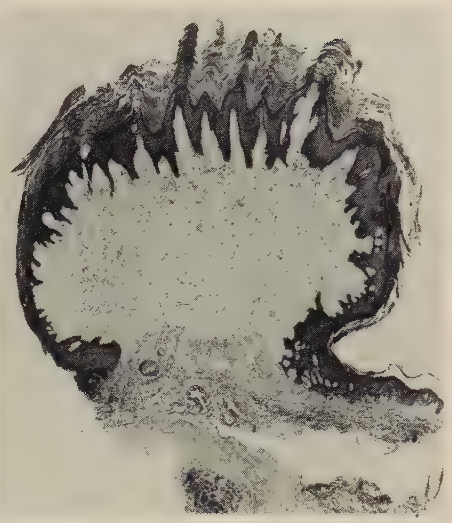
POLYPS, CYSTS, KERATOSES



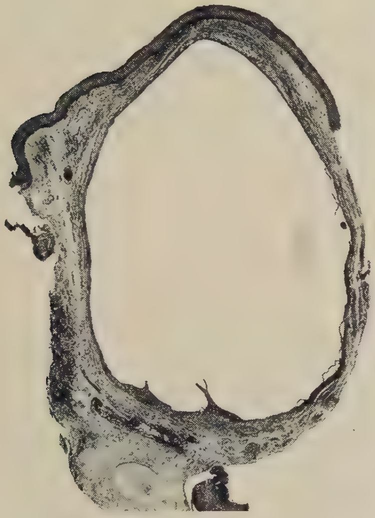
Fibrous polyp of keloid character in vestibule. Collagenous fibrous tissue. x 10.



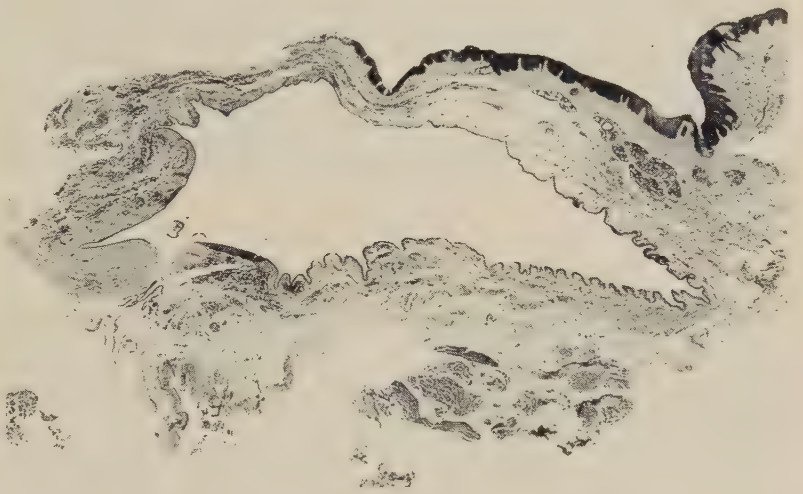
Polypoid fibrous fold of mucosa in vestibule; hyperplastic epithelium. x 16.



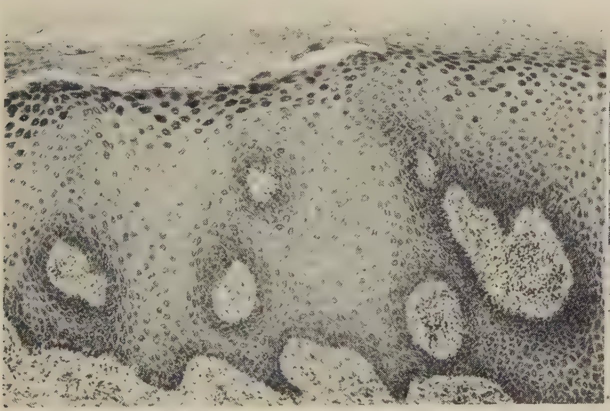
Vascular fibrous polyp on cartilaginous septum; marked acanthosis and hyperkeratosis of epithelium. x 10.



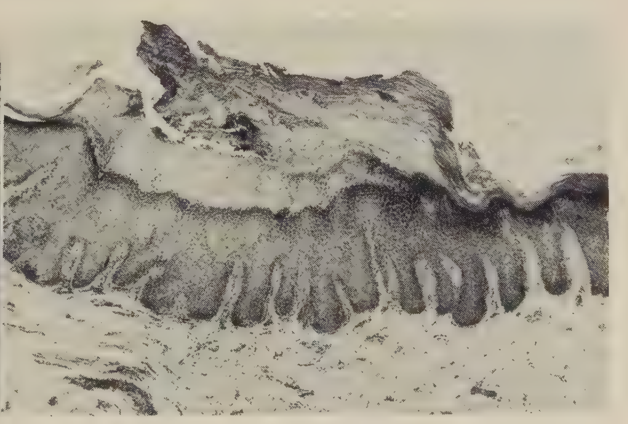
Mucous retention cyst on upper septum of anterior nares. x 15.



Mucous retention cyst from floor of posterior vestibule. x 14.



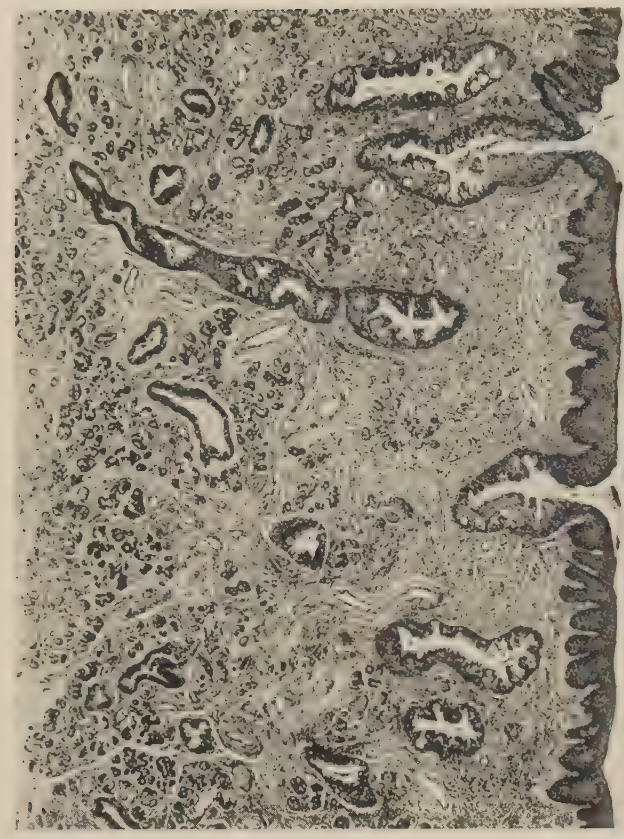
Acanthosis and parakeratosis; clinically a white plaque in Kiesselbach's area. Not leukoplakia. x 75.



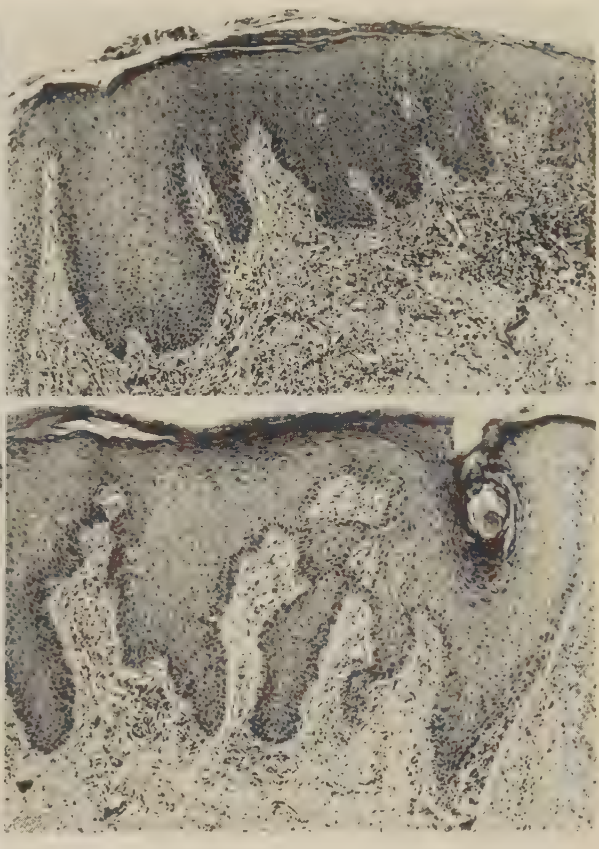
Focal hyperkeratosis on anterior nasal septum. "Warty," clinically. x 48.

EPITHELIAL CHANGES IN NASAL MUCOSA

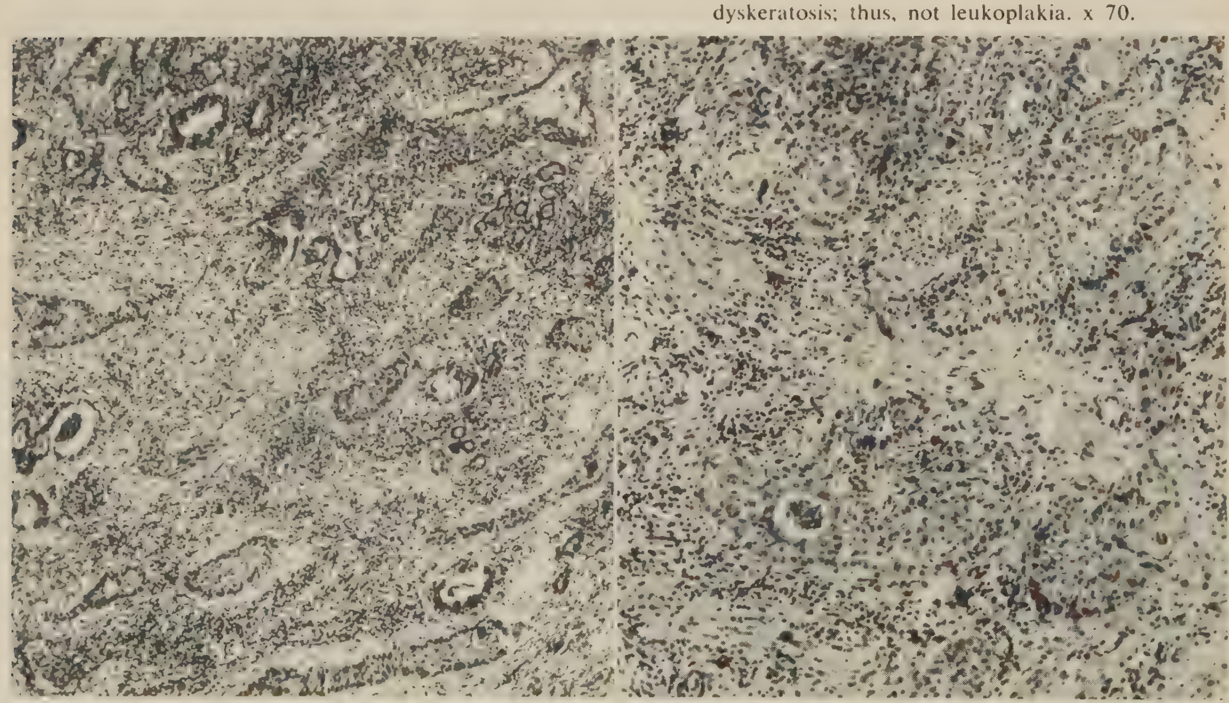
METAPLASIA–HYPERPLASIA



Metaplasia. Stripped hyperplastic nasal mucosa, full thickness. Squamous metaplasia of surface epithelium extending into ducts. x 31.



Metaplasia and hyperplasia. Septal mucosa in chronic rhinitis diagnosed leukoplakia. Squamous metaplasia with marked acanthosis and exaggeration of rete pegs, but no dyskeratosis; thus, not leukoplakia. x 70.



Metaplasia versus neoplasia. Squamous metaplasia of epithelium extending into seromucinous glandular elements suggested an invasive tumor. The picture is further complicated by dense cellular exudate. x 75, x 125.

CHAPTER 18

TUMORS OF THE NOSE AND SINUSES

If inflammatory polyps are excepted, benign tumors of the nose and sinuses of man are comparatively rare, although chondroma arising in the ethmoidal region is not rare if the number of reports of such tumors in the literature can be taken as an indication. Menne and Frank, in 1937, reviewed 47 cases, including one of their own, and commented on their slow growth and benign clinical course. Their case, however, showed the same persistent destructive expansion and involvement of neighboring cavities as the case included in the section on malignant tumors of nose and sinuses. In Hickey's case, in which the tumor was removed surgically, apparently in an early stage, no evidence of recurrence could be seen at the end of two years. Howarth reported a chondroma arising from the anterior part of the septum and having no relation to the ethmoid. This is a very rare site. The tumor usually begins in early adult life; it is not the result of trauma, but apparently has its origin in cell rests in osteogenetic areas of the bones.

The incidence and characteristics of the more common benign tumors have been discussed in Chapter 8. There are, however, several tumors both benign and malignant that are so specific to an anatomic part that they are discussed in the section dealing with that part. Hemangioma of the nasal septum, the epithelial papilloma, and the neural tumors of the nose and nasopharynx will be included in this section. It is also convenient to discuss here the tumors and cysts that arise in the maxilla and mandible. Dysplasias of those bones are described in Chapter 6.

One of the difficulties in presenting the subject of tumors of the nose and sinuses on an anatomic basis is that often the site of origin is obscured by the time a case comes to observation. The nasal and sinus cavities are so intimately associated that it is easy for a tumor arising in one part to gain access to another. This applies not only to malignant but also to benign tumors and brings the two closer than is usual so far as dangerous potentialities are concerned. In addition, several of the most important tumors actually arise in the supporting bones and not in the nose or sinuses, but have ready access to the cavities of the sinuses and nose. This is particularly true of tumors originating in the maxilla, such as benign giant cell tumors, ossifying fibroma, and osteogenic sarcoma, which by erosion of the delicate bony septa invade the orbit, ethmoidal sinuses, and nasal cavities. Meningioma of the anterior cranial fossa may erode into the orbit, nasal cavities, sphenoidal or ethmoidal sinuses. Illustrations of such a tumor are included in the following plates. The patient was a 45-year-old woman from whose frontal fossa a meningioma had been removed six and a half years previously. The tumor also invaded the orbit, frontal and ethmoidal sinuses, and x-rays showed extensive destruction of the bony walls of these cavities.

SPECIFIC TUMORS OF THE NOSE

Hemangioma of the nasal septum (bleeding polyp) is a berry-like lesion developing, as a rule, on the septum anteriorly, in or near Little's area. It occasionally occurs in other portions of the nose and in the accessory sinuses. It bleeds readily, and epistaxis is practically always the initial symptom. It is subject to trauma and therefore commonly has an ulcerated surface. The history is usually of only a few months' duration. Clinically it is necessary to differentiate the tumor from an area of bleeding granulation tissue which has resulted from an ulcerative inflammation.

This tumor may develop at any age and there is no significant difference in its distribution between the sexes. In 17 cases in the Registry recently analyzed, the ages of the patients ranged from 16 to 70 years; 9 were male and 8 were female. In every case the site was the region of the bone-cartilage articulation of the septum. Of special interest was the development of a tumor in one patient during the fifth month of pregnancy. As a complication of pregnancy the tumor in this location is uncommon.

The purist will criticize the reference to this lesion as a neoplasm, and perhaps with some justification. It is, however, an aggressive tumor-like growth of blood vessels that is unlike granulation tissue both clinically and histologically. Such terms as bleeding polyp and vascular granuloma are not sufficiently specific for this definite clinical entity.

Histologically, the tumor consists of a mass of blood vessels of various sizes, usually with little connective tissue stroma. In the presence of ulceration there is active polymorphonuclear leukocytic infiltration. The picture is indistinguishable from that seen in the other vascular-tumor entities, i.e., granuloma pyogenicum, pregnancy tumor and vascular nevus, discussed in the chapters on hemangiomas. The history, particularly as to location, is necessary in order to name it specifically. Removal is often followed by recurrences, which can be avoided if excision is carried out with ample margin and with cauterization of the cartilaginous base.

Epithelial Papilloma (Papillary Epithelioma) of the Nose.—This name is not particularly good because all papillomas are epithelial and this particular tumor is not as papillary as the general run of orthodox papillomas. This is the term applied to it by Ewing and as long as its connotation is generally recognized, it will serve. It is such a typical lesion histologically and clinically that it is necessary to separate it from the papillomas on the one hand and the polyps on the other. Willis calls it papillary respiratory epithelial carcinoma, but of over 40 cases in the Registry only one so far has been frankly malignant. Local recurrence after removal, however, is not uncommon. The histologic appearance of these recurrences is identical with that of the original tumor. One of these recurrent cases has been followed for six years and another for ten.

The lesion occurs most commonly in the adult male, and from the middle turbinate toward the posterior portion of the nasal cavity. It also arises on the septum and occasionlly in a sinus. One instance of origin in the maxillary sinus is included in the Registry material. The tumor may be multiple, but not with the frequency of nasal polyps. Its clinical appearance varies. It may be papillomatous, polypoid, lobulated or verrucous. It has a firmer consistency and a thicker, rougher surface than the common polyp. The tendency to bleed, so common in other nasal lesions, is lacking, and the initial symptom is nasal obstruction rather than epistaxis.

The pathogenesis of the lesion, despite its specificity, is not known. Waltner's recent report of regression of the lesion in a number of cases treated with heavy dosage of aureomycin suggests an inflammatory component. But it is obviously not entirely inflammatory, and it certainly has neoplastic features.

The histologic appearance is characteristic, and even when the stroma is polypoid, the convoluted surface of a thick layer of stratified epithelium identifies its nature. The epithelium is predominantly transitional in type, but it does vary, not only in different tumors but in different areas of the same lesion. It is cuboidal, columnar, transitional, or frankly squamous and varies from 7 to 40 cells in thickness. The basement membrane is intact and does not have the hyalinized thickening so frequently seen in ordinary nasal polyps and in the mucosa in chronic allergic states. A certain degree of dyskeratosis and hydrops of individual cells is common, and there may be minute leukocytic collections in the epithelial layer. The dyskeratosis is of Bowen and leukoplakic type with about equal frequency and can be so striking as to justify the diagnosis of "carcinoma in situ" for those who care to use that ambiguous term. Normal glands are practically absent, but pseudoglands often develop from infolded epithelium. Cysts of any type are never present to the extent seen in inflammatory polyps. The supporting stroma is a loose vascular connective tissue in which there is usually some degree of plasma cell and lymphocytic infiltration. In the Registry cases, eosinophils were present in more than half the lesions and an occassional secondary lymphatic follicle was found.

Neurogenic Tumors.—The majority of these arise in the roof of the nose, but they are found also in the nasopharynx. There are two general types, one that develops from peripheral neural elements and belongs to the peripheral neurilemomas or ganglioneuromas found in association with peripheral nerves elsewhere, and those of central or neural crest origin. The former contains in varying proportions neurofibrous, neurilemmal and nerve-cell elements. Its histologic character, therefore, varies greatly and confusingly in different tumors. In one the neurilemmal element will predominate, including the typical palisading of the cells, and its identity is evident. In others the ganglion cell is the prominent feature, and in its more primitive forms its identity may not be clear.

Rare tumors have been reported, largely in the form of individual case reports, as primary intranasal neuroblastoma, *esthesioneurocytoma olfactif, esthesioneuroepithelioma olfactif,* etc. Berger, Luc and Richard described the first case in 1924, and considered their tumor, which had features of both central nervous system and sympathetic system neuroblastomas, to have origin from a stem cell, the esthesioneuroblast of the olfactory placode. Most authors have supported the probable placodial origin of these tumors, but some favor a source in sympathetic elements of the nasal mucosa, and one suggestion of possible origin in Jacobson's organ has been made. Unlike reported neuroblastomas in other locations, which occur predominantly in children, these tumors have occurred in adults and have been successfully treated by irradiation, or surgery and irradiation. They have presented as firm obstructing polypoid masses with attachment high in the nasal cavity, usually in the region of olfactory mucous membrane.

There is an additional category of lesions that are really not tumors, but that result from maldevelopments. A portion of the frontal lobe may escape through a defect in the cribriform plate or through the ethmoidal sutures and present in the nose, or subcutaneously at the base of the nose. Such "tumors" are readily recognized histologically because they retain the brain-cortex elements. These may be apparent at birth because of the external deformity at the base of the nose, or as a nasal polyp. One of the latter presenting in the external nares at birth and attached by a long thin pedicle to the roof of the nose is shown in the following illustrations. These lesions are entirely benign.

The neurogenic tumors behave clinically about as do the other tumors of the nose and paranasal sinuses. They invade and erode, eventually involving the bony cavities with the same persistence. They metastasize rarely, however, and are not as sensitive to irradiation therapy.

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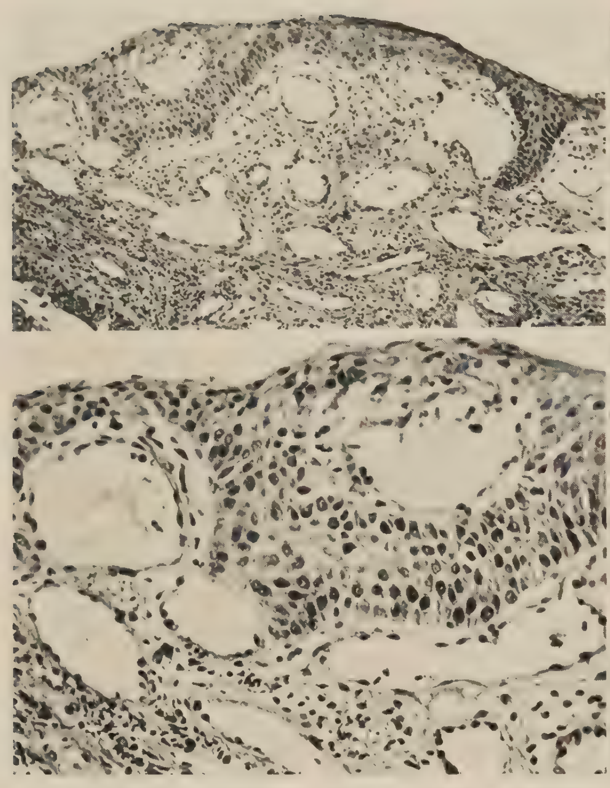
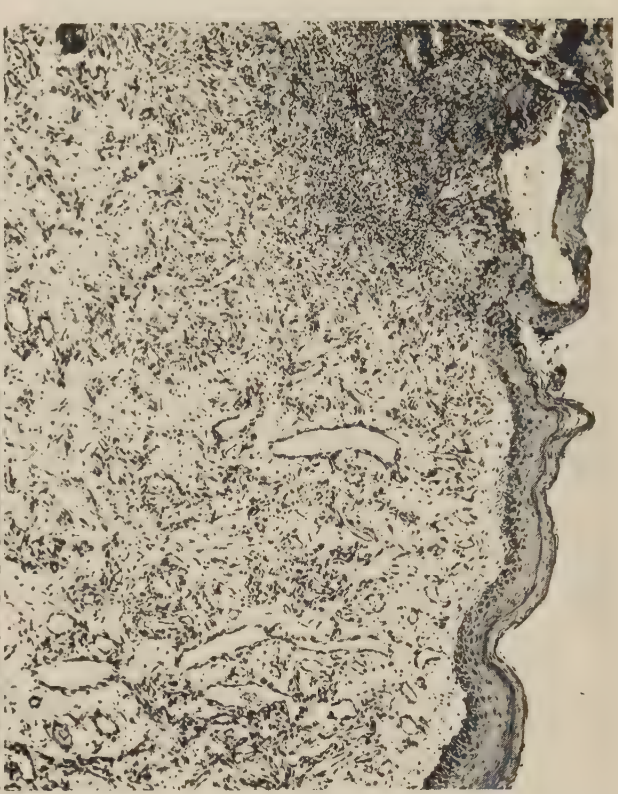
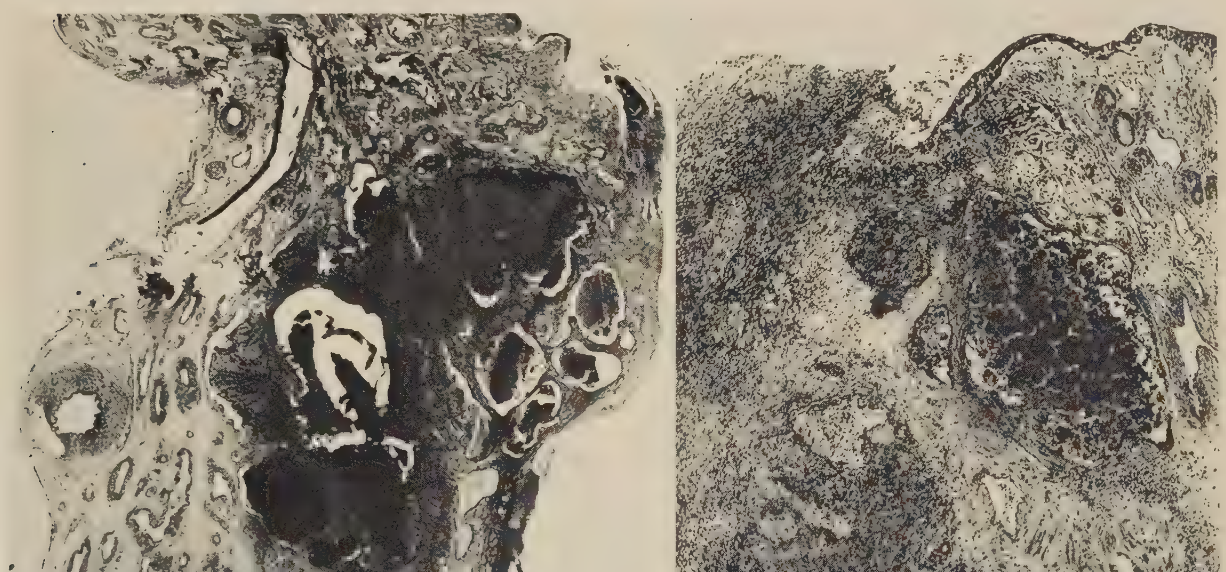


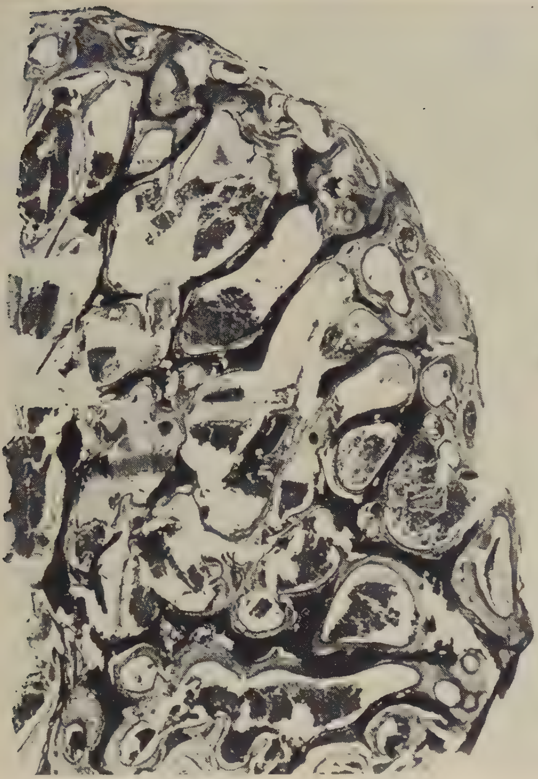
Telangiectasia of unknown etiology, possibly hereditary. Dilated, thin-walled vessels without evident proliferation, in nasal mucosa of patient with history of repeated severe epistaxis. x 48, x 165.



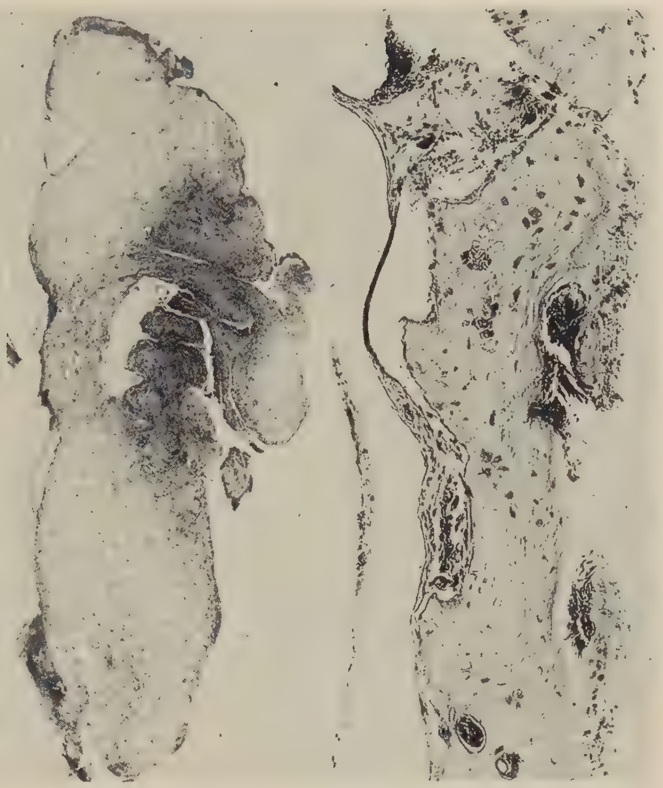
Granulation tissue polyp, that caused profuse bleeding in contrast to preceding lesion. Actively proliferating capillary vessels have an oriented pattern. Ulceration at top. x 70.



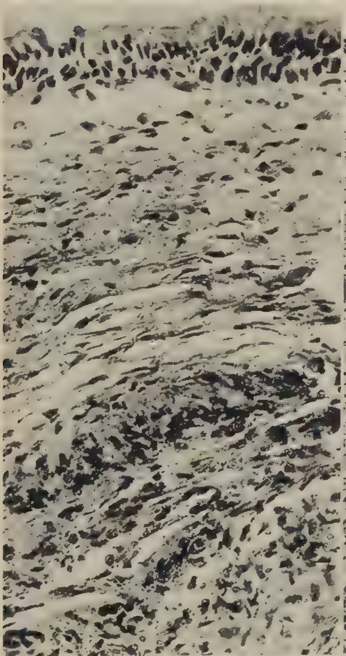
Telangiectasia or varices of turbinate in a man with portal cirrhosis and arteriosclerosis, who died of nasal and pharyngeal hemorrhage. Possibly related to excess of circulating estrogens.



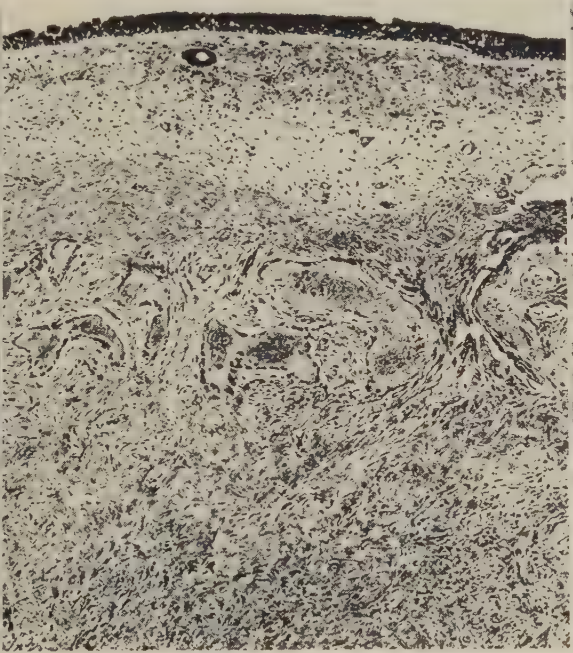
Cavernous hemangioma from floor of nose of 74 year old woman. Unusual lesion because of associated bone. x 13. (L. G. Richards, Boston.)



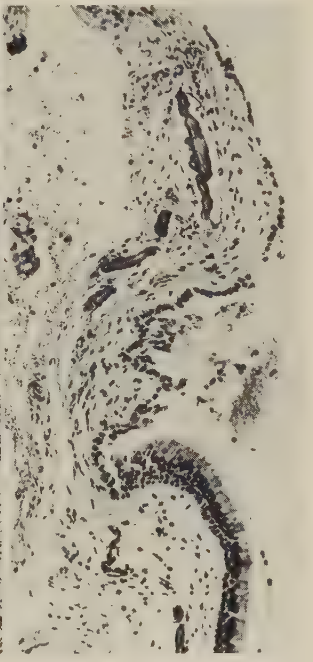
Organizing hemorrhage within thickened mucosa of frontal sinus and adjacent bone, removed from jet pilot five weeks after a rapid descent—aerosinusitis. x 11, x 100. (R. W. Marks, Walnut Creek, Calif. and D. L. Poushter, USAF [MC].)



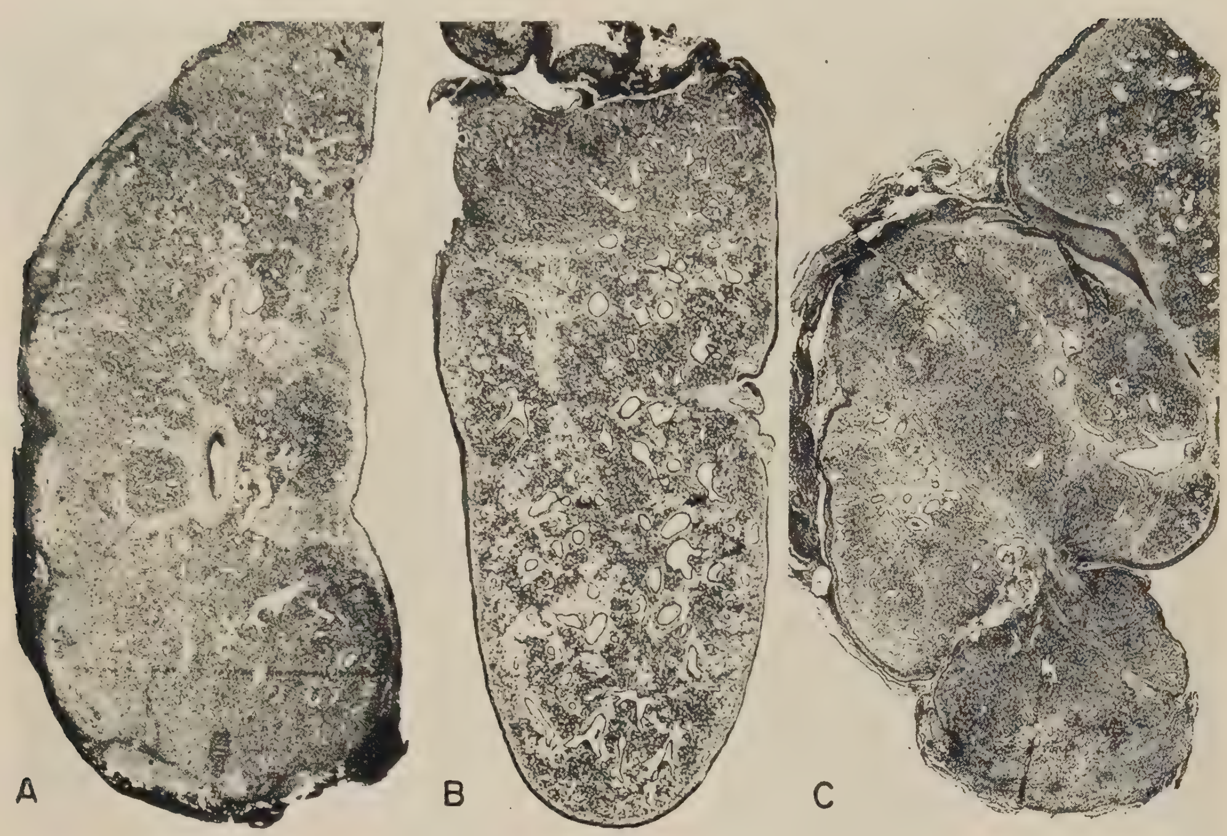
Hemosiderin, in magnified field of frontal sinus mucosa of same pilot. **A,** x 235.



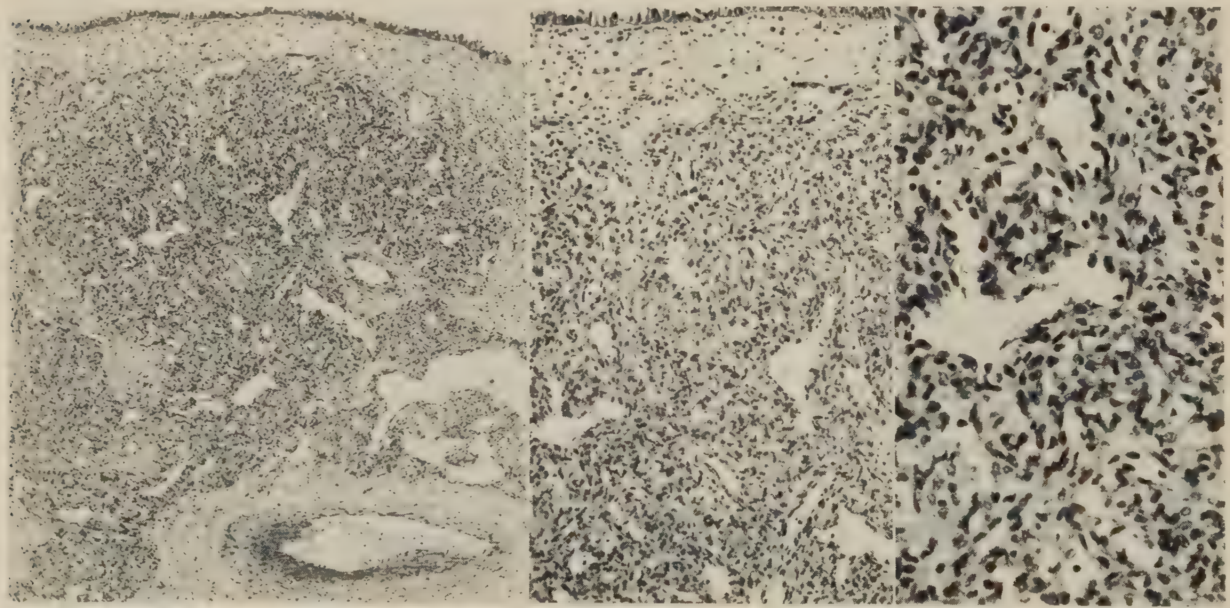
Organizing hematoma (another case) in mucosa of frontal sinus with osteoid bone formation. **B,** x 70. (There is definite history of trauma in some "osteomas" of the paranasal sinuses.)



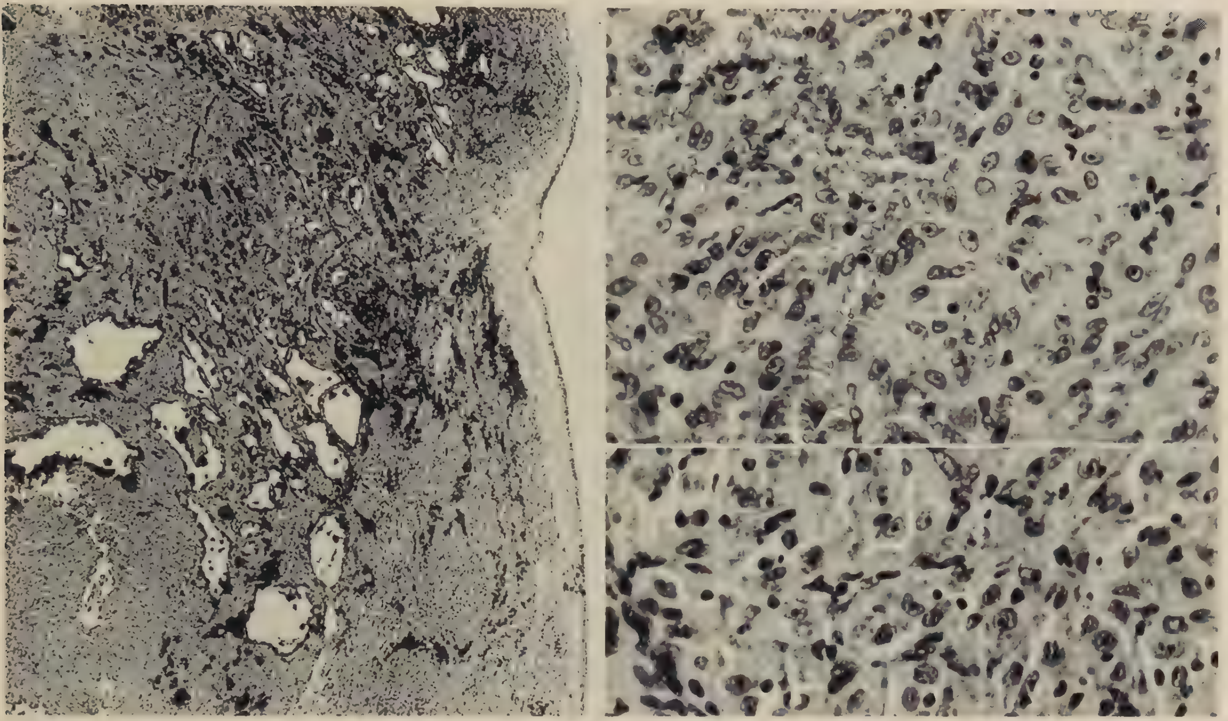
Calcific deposits within maxillary sinus mucosa are sometimes in cylindroid form. **C,** x 125.



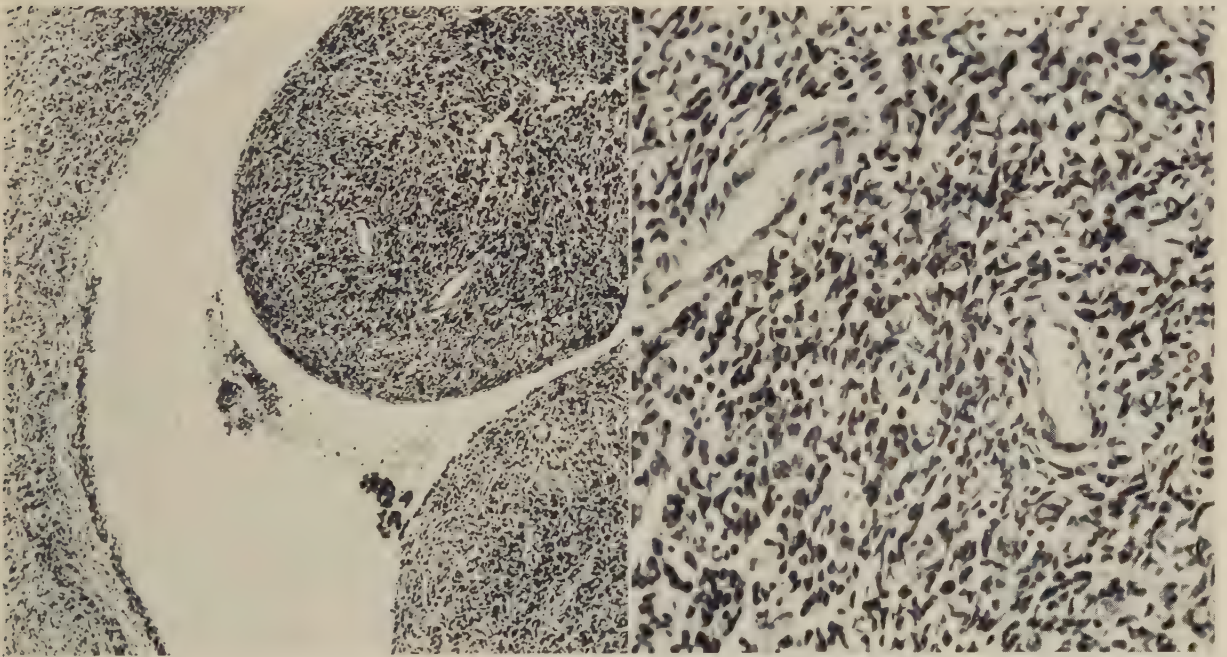
Vascular intransal lesions, usually polypoid but sometimes sessile, occur most commonly on the nasal septum. They are made up of aggregations of capillaries which appear to be proliferating from larger vessels, thus sometimes presenting a partially lobulated pattern **(A** and **C).** When surfaces are ulcerated as in **A** and **C,** histologic features of granuloma pyogenicum are indistinguishable from those of capillary hemangioma. Clinical history of only 1 to several months' duration tends to favor diagnosis of granuloma pyogenicum. All approximately x 20.



Details of **A.** Endothelial cells and tiny capillaries proliferating from larger vessels form a pseudolobule *(left).* Inflammatory cells (plasma cells, lymphocytes and a few polymorphonuclear leukocytes) and stromal fibroblasts contribute to the evident cellularity. x 48, x 90, x 205.



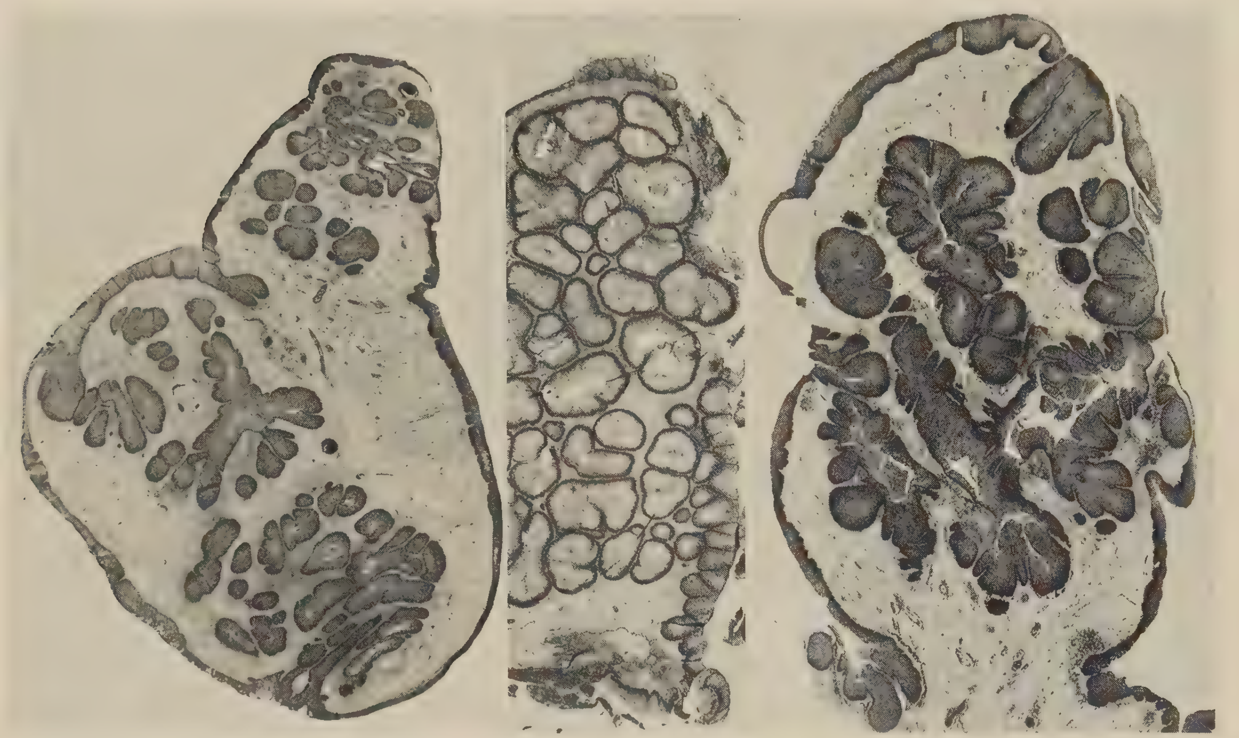
Hemangioendothelioma of the nasal septum of a 16 year old girl caused severe epistaxis, and recurred two months after removal. *Left,* disorderly proliferation of capillary vessels, a few cavernous, in very vascular portion of tumor. x 25. *Right,* in solid areas large swollen endothelial cells, some atypical, partially or completely fill the lumen of capillary spaces. Occasional mitoses. x 325, x 360. The endothelial cells lie inside of the reticulin sheath of the capillary vessels, in silver impregnated sections.



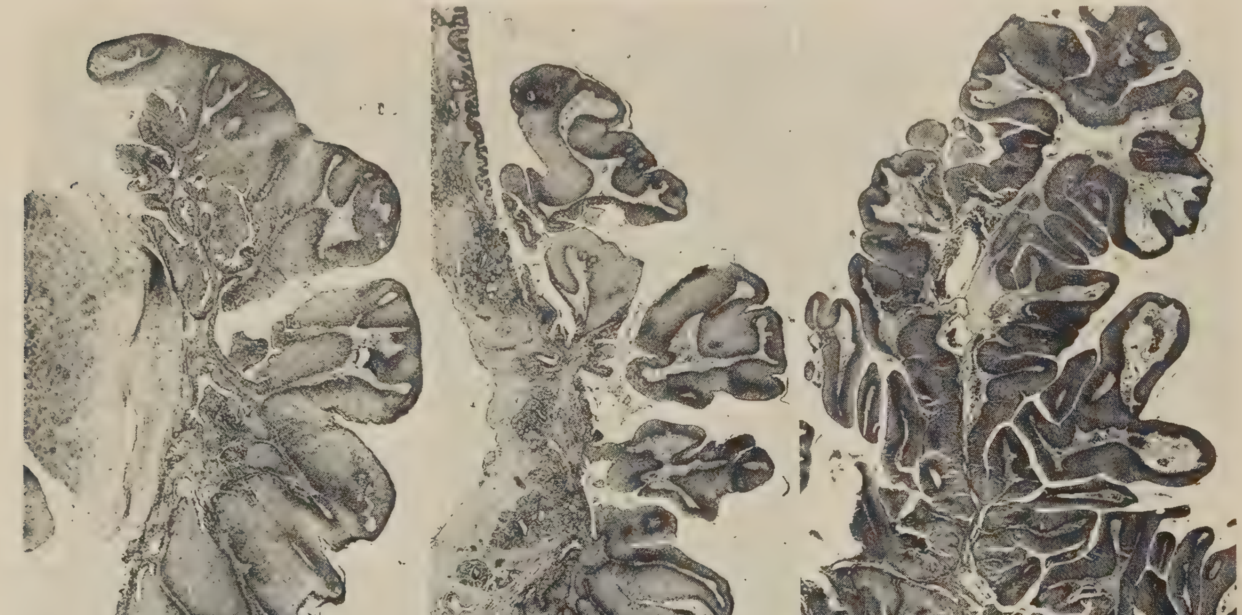
Hemangiopericytoma. Again the discernible vascular element is limited since most of the capillaries are collapsed. Endothelial cells are normal. The proliferating cell is considered to be the "pericyte of Zimmerman"; it is rounded, oval, or elongated. x 83, x 274. Reticulum stains demonstrate its location outside of the reticulin sheaths of the capillary vessels.

PAPILLOMA, NOSE AND PARANASAL SINUSES

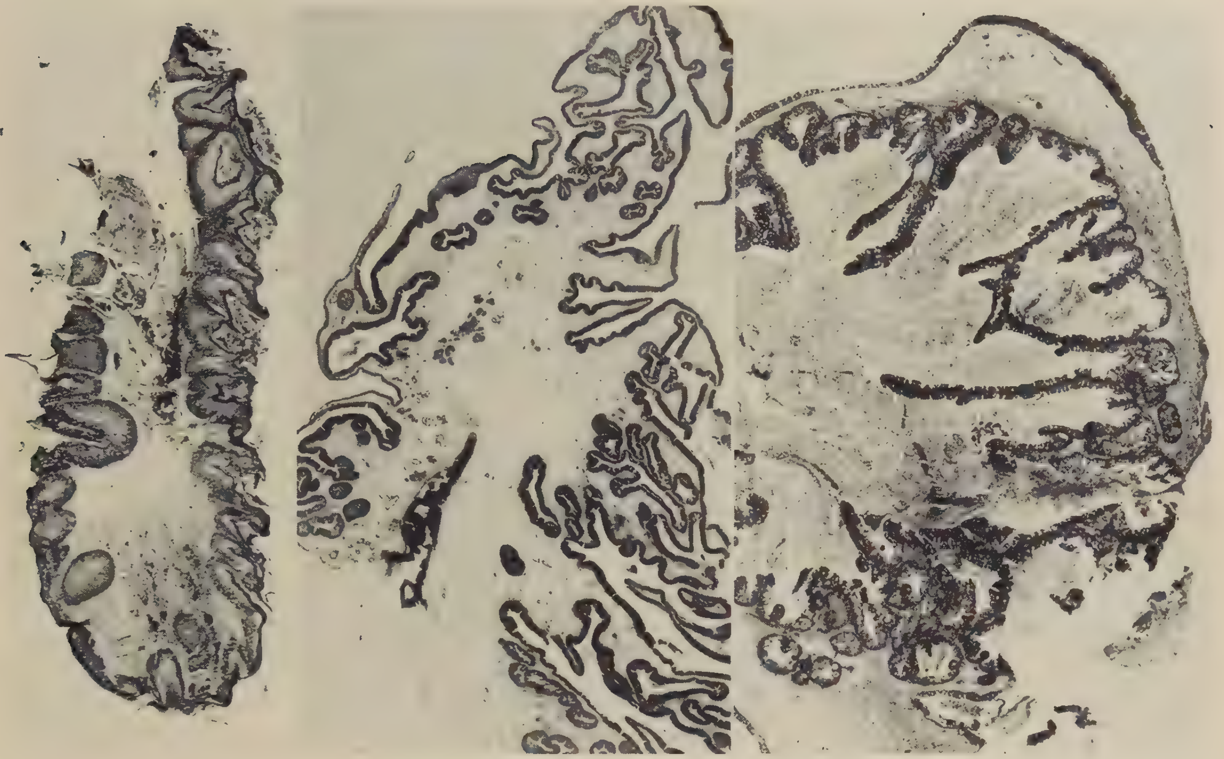
(EPITHELIAL PAPILLOMA)



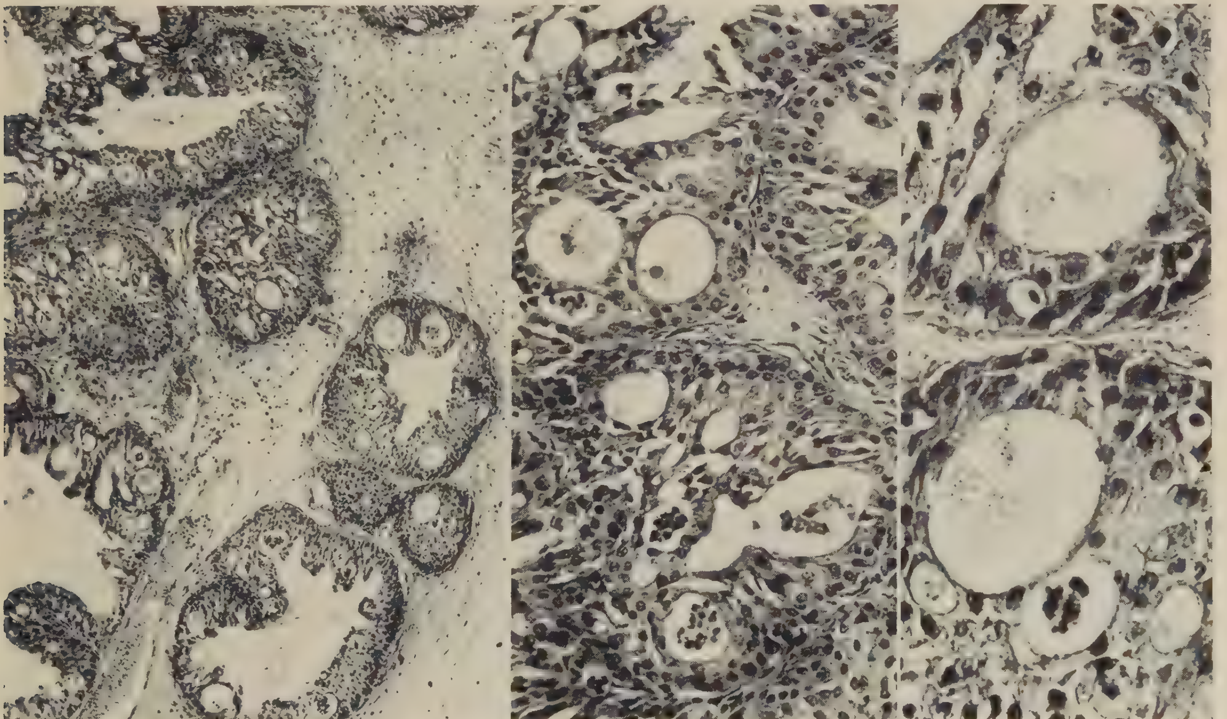
Polypoid masses of the inverted papilloma type occur most frequently in the nasal cavity, ethmoid and antrum. The epithelium may be respiratory, or squamous or varying transitions between the two. Note the abundant edematous stroma and polypoid configuration. x 9, x 12, x 10.



Papillomas (of nasal septum, *left* and *center*) with very little stroma and more branching papillary growth. Hyperplastic, usually nonkeratinized, epithelium of so-called transitional type. Specimens from the same patient may include different patterns of growth. x 17, x 14, x 12. Multiple recurrences of these lesions are common.

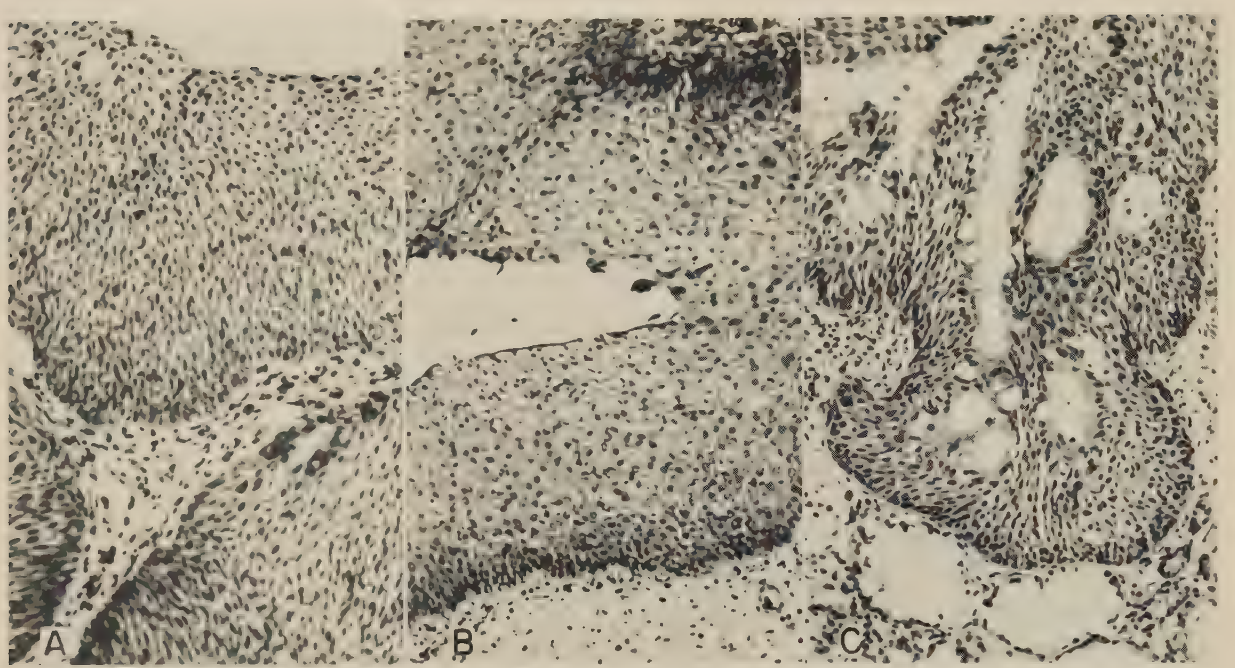


Other examples of the papillary lesion. *Left,* rarer squamous cell type and well defined granular cell layer and marked hyperkeratosis. x 13. *Center* and *right,* "transitional cell" and respiratory epithelial variants in specimens from patients with other lesions like those on preceding plate. x 12, x 15. The reaction has been attributed to inflammation, and a virus etiology has been suggested.

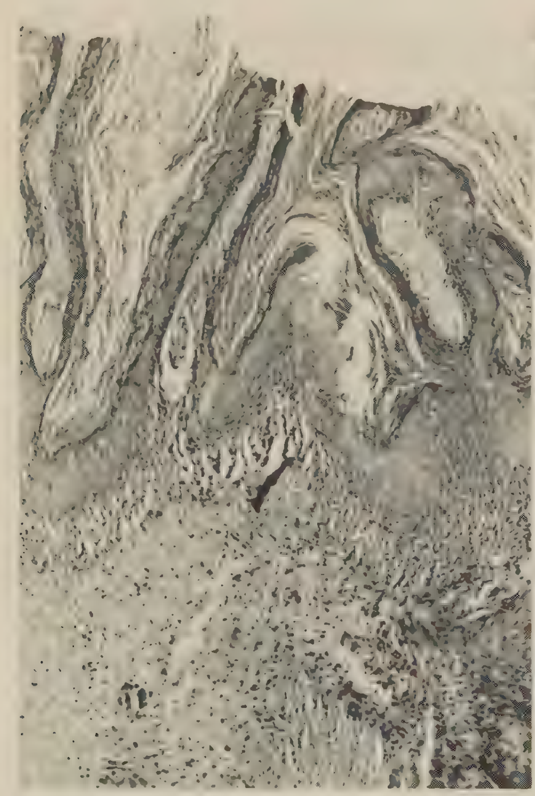


Details from section at *upper right.* Evidence of inflammation, noted here, is present in some but not all papillomas. Intraepithelial clusters of leukocytes, inspissated mucus, and granular debris can be seen, but no convincing virus inclusions have been demonstrated. These cysts have been mistaken for parasites and fungi. x 70, x 185, x 395.

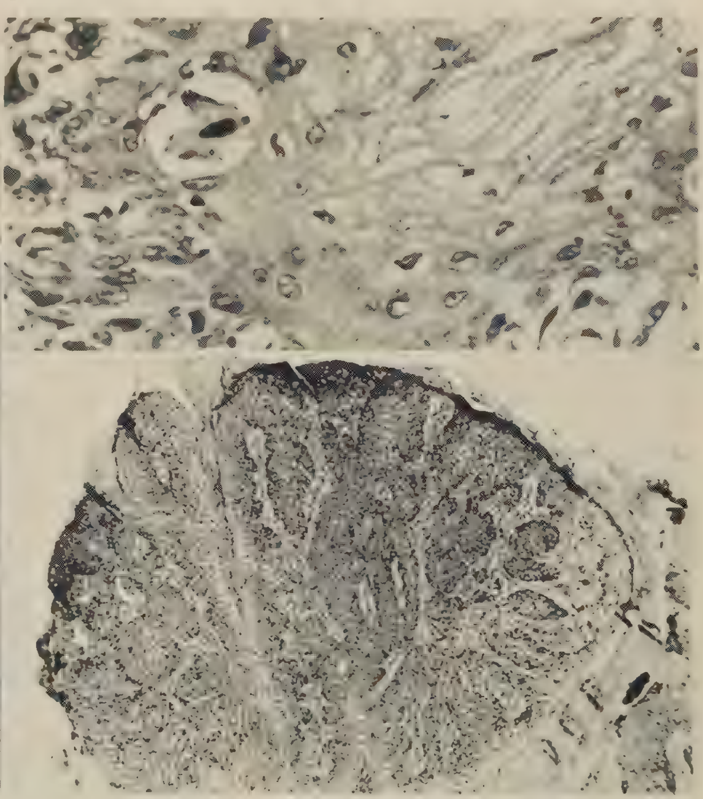
EPITHELIUM



The surface epithelium may occasionally be frankly squamous, as below and on preceding plate. Most frequently it is of intermediate cell or cylindrical cell type (A, x 145), which may be hydropic (B, x 90). C. Mucous cells may still be present as nests in proximal portions of involved ducts, or scattered individually or in small clusters in the surface epithelium. x 160.

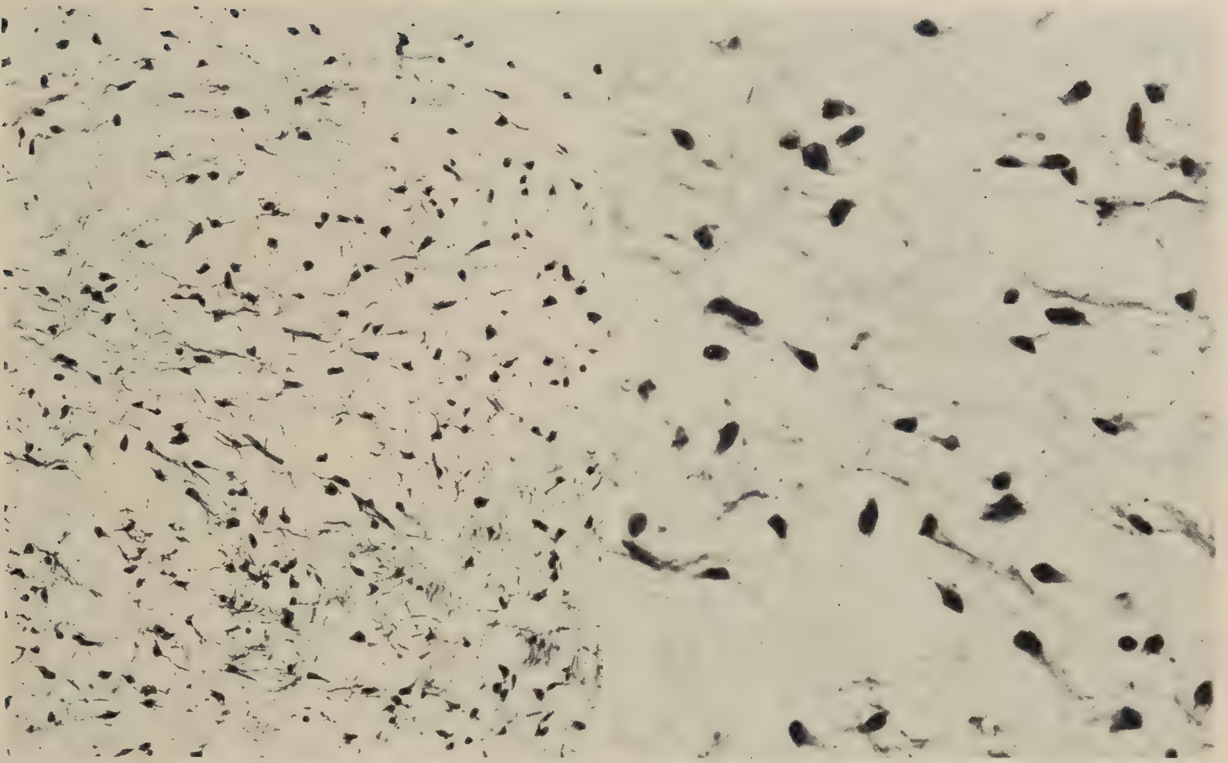


Hyperkeratotic squamous epithelium covered only one of multiple papillomas in an adult female. This extreme form is unusual in nose and paranasal sinuses. x 60.

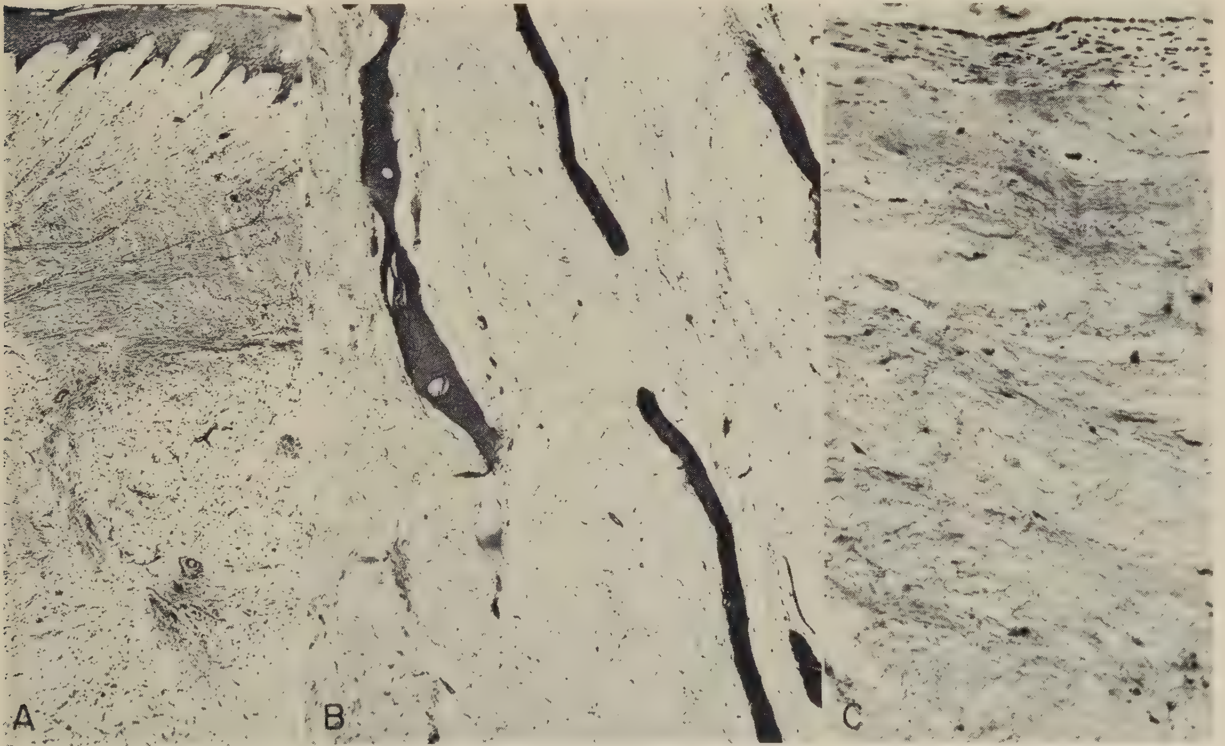


Malignant dyskeratosis. Leukoplakic foci *(upper)* are not infrequently misinterpreted as carcinoma. x 350.

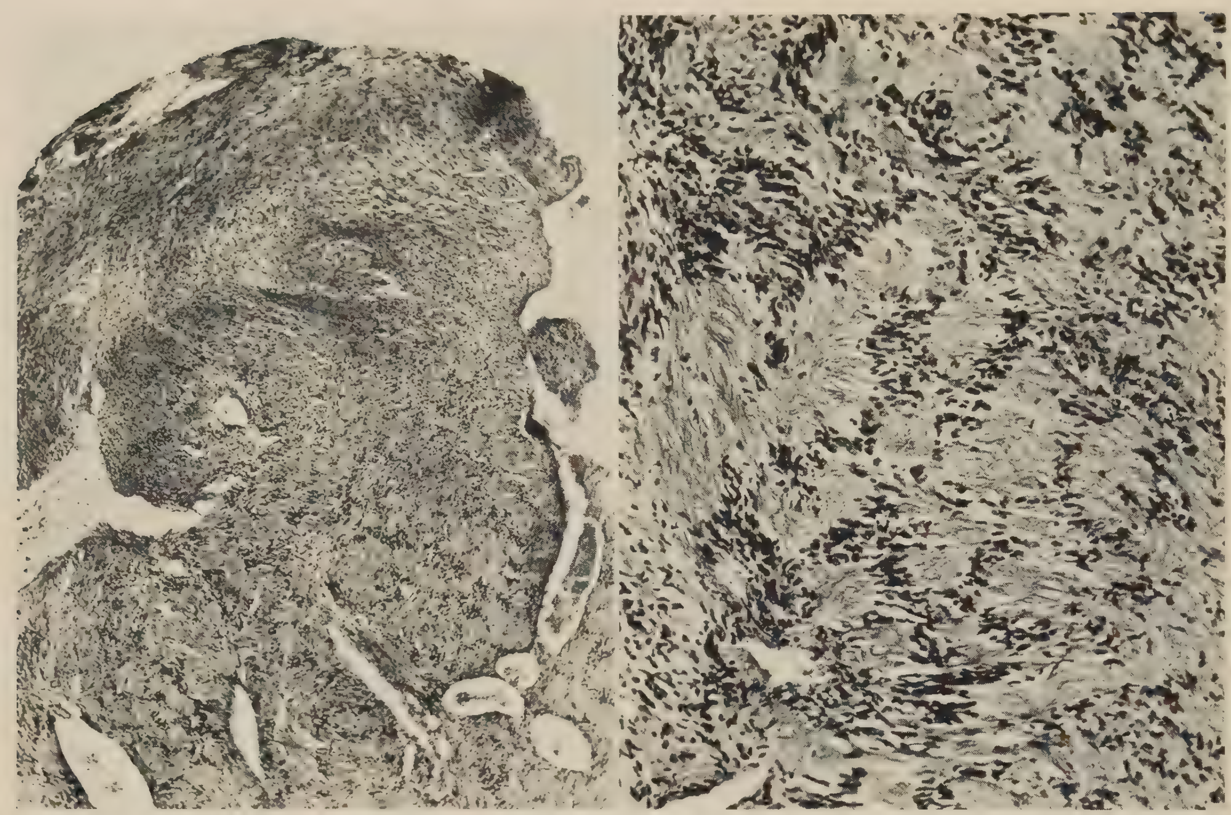
Squamous cell carcinoma developing in an epithelial papilloma *(lower)*. This is not *un*common in older patient. x 50.



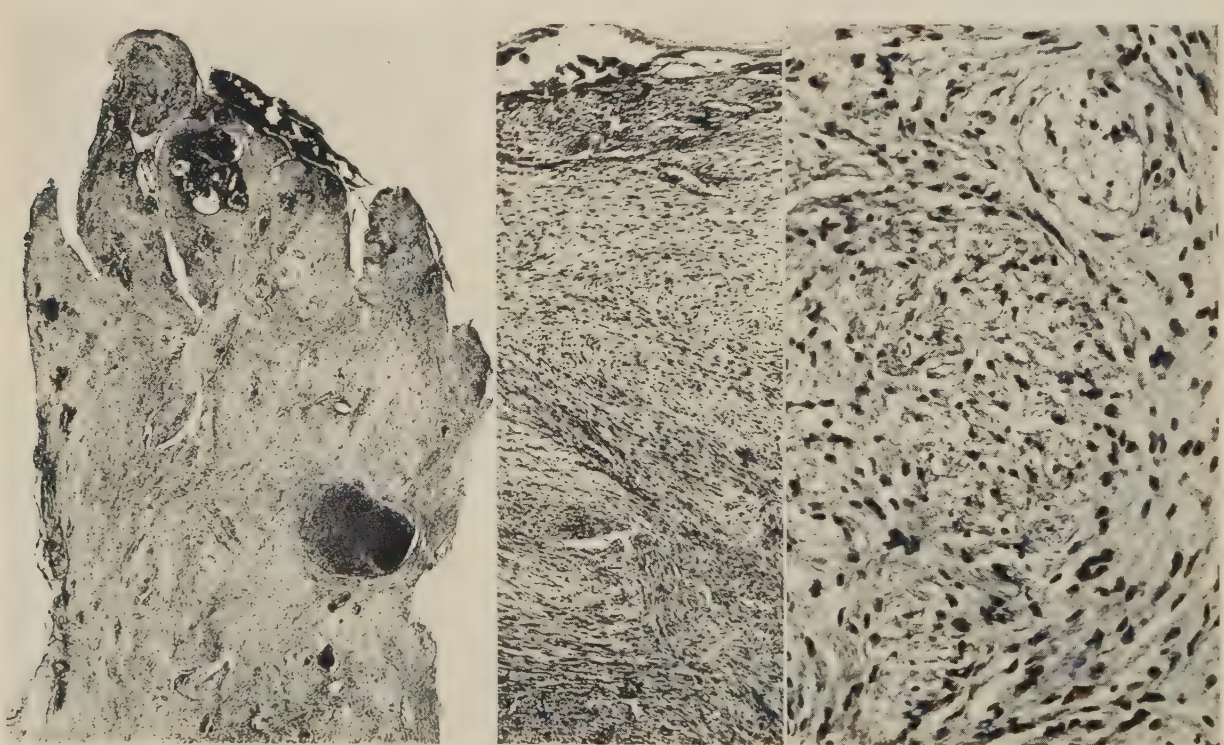
Fibromyxoma, in maxillary sinus of a young man, resembles embryonal mesenchyme with its stellate cells, delicate fibrils and mucinous intercellular substance. The tumor eroded through floor of orbit into alveolar process. Metastasis is unlikely. x 210 and 545.



A. **Fibromyxoma** (same case as above) under oral mucosa. x 48. B and C. A similar tumor, but less cellular and with a smaller mucoid content. B. Invading the bone, it causes atrophy and necrosis of the trabeculae. x 48. C. It has replaced the gingiva and reached the epithelial surface (at top).

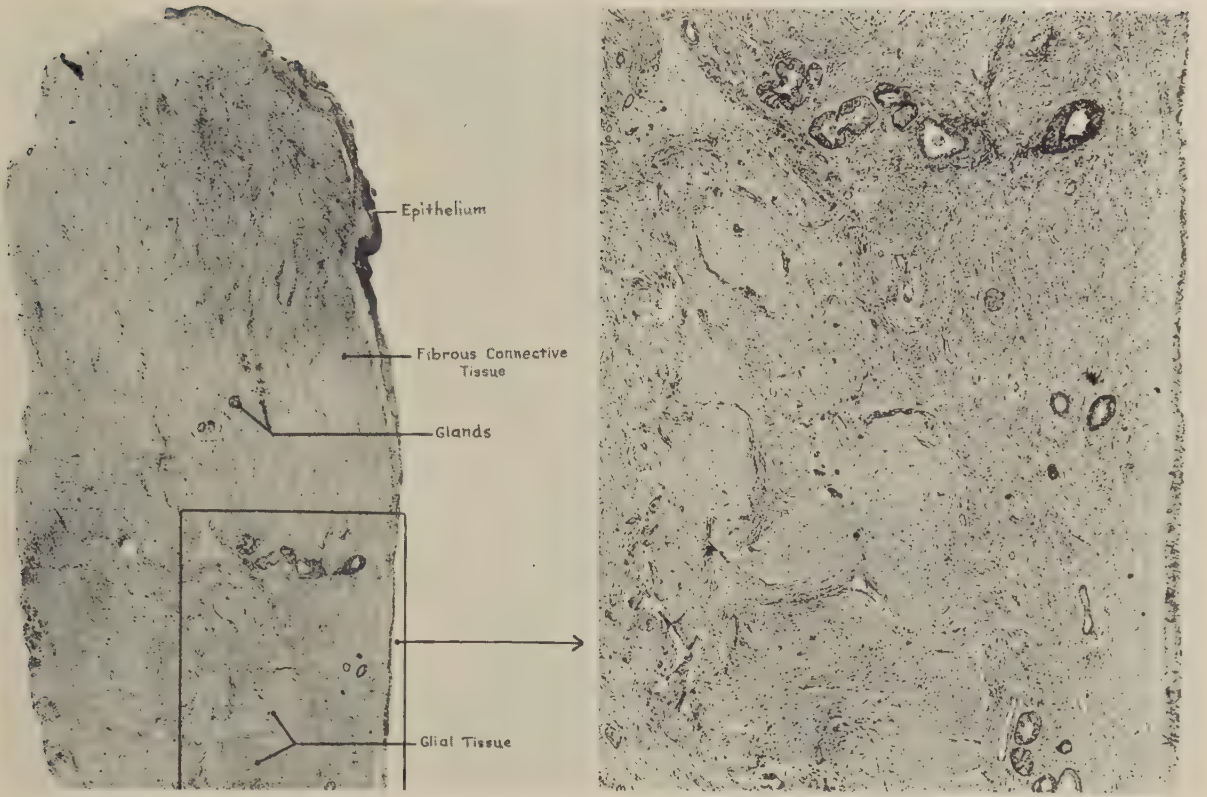


Neurilemoma, nasal cavity; extension of tumor of nasolabial fold, four months' duration, in 21 year old man; painless. A lobulated mass made up of neurilemmal fibers, the nuclei of which have an organoid degree of palisading. x 48, x 125.

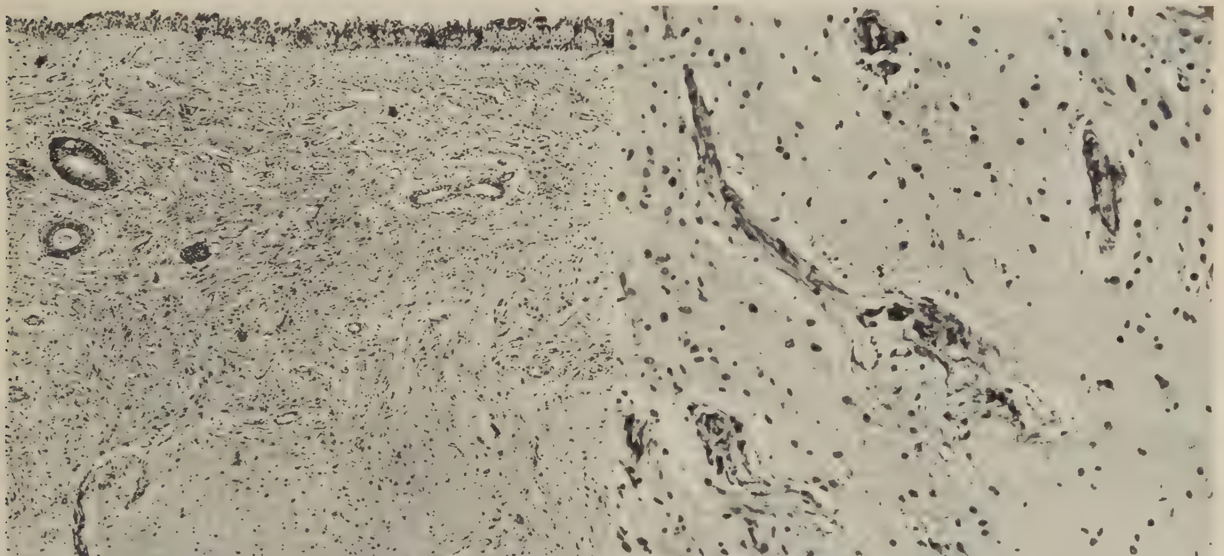


Neurofibroma, nasal cavity. A pedunculated but solid mass made up of interlacing bundles of uniform fibres, the nuclei of which show little, if any, palisading. x 13, x 48, x 205. This is the Antoni A type of tumor.

GLIOMA, NOSE
(ENCEPHALOCELE)

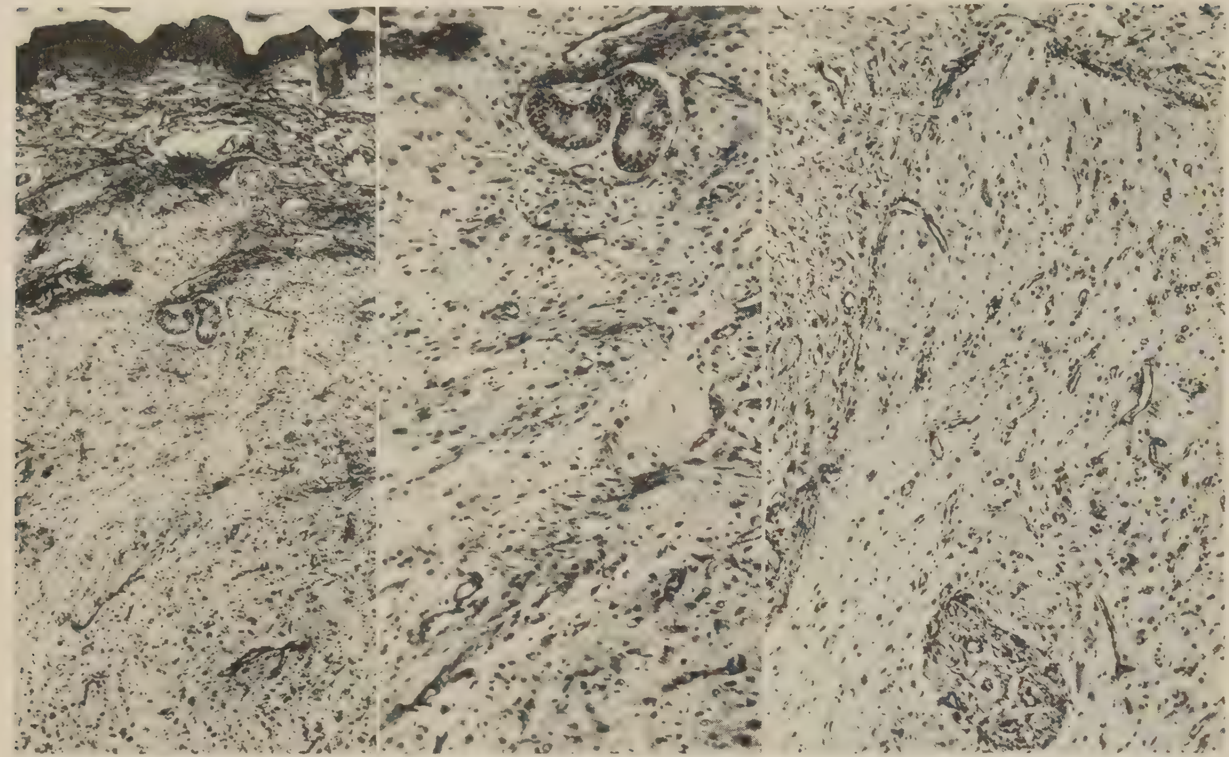


A pedunculated mass that presented through nares of a newborn infant. It was attached by thin pedicle to roof of nasal cavity and was removed without difficulty. It is made up of a convoluted mass of glial tissue that has pushed the nasal mucosa ahead of it. The difference between the two tissues is readily seen. x 11, x 30.

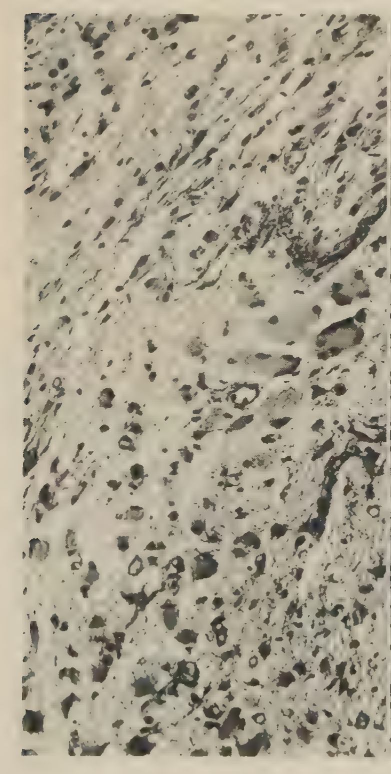


The resemblance to brain cortex is evident, although no nerve cells are included. The cells are glial astrocytes. x 48, x 114. This is not a neoplasm, but a congenital extrusion of central neural elements into the nasal cavity.

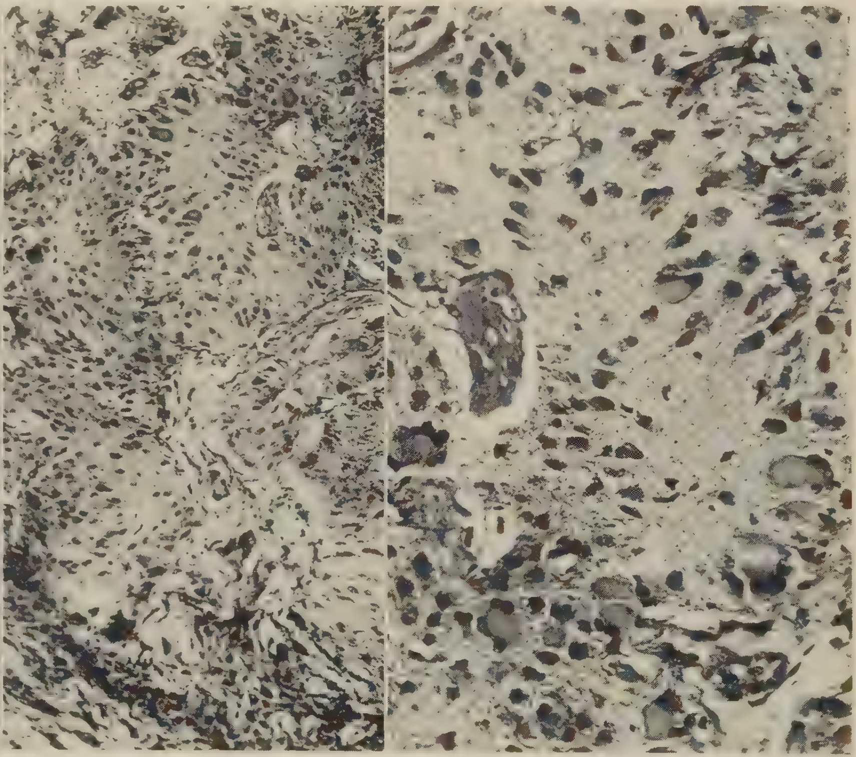
HETEROTOPIC EXTRANASAL AND INTRANASAL FIBROGLIAL TISSUE



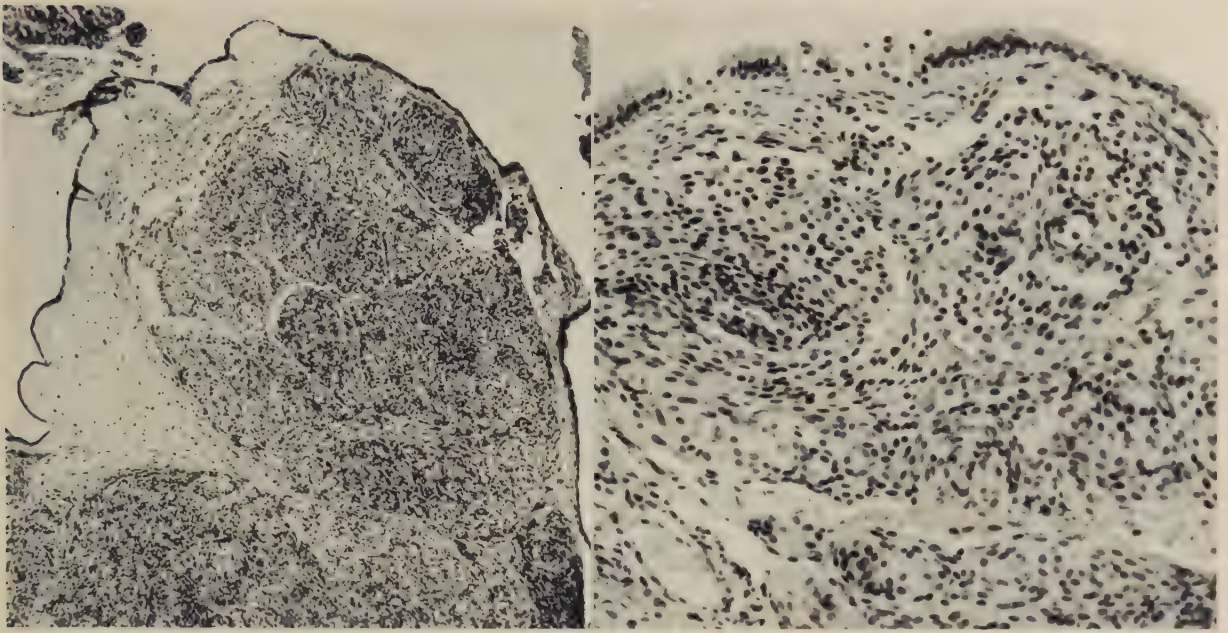
A, B & C. **Heterotopic neural tissue.** Tumor that had been diagnosed dermoid cyst was removed from bridge of nose of a 5 months old infant. A. While not encapsulated, it is expansile rather than infiltrating and is approaching the skin surface. x 48. B & C. It is a well vascularized mass of fibroglial tissue. x 90, x 75. (Also see D, left below.)



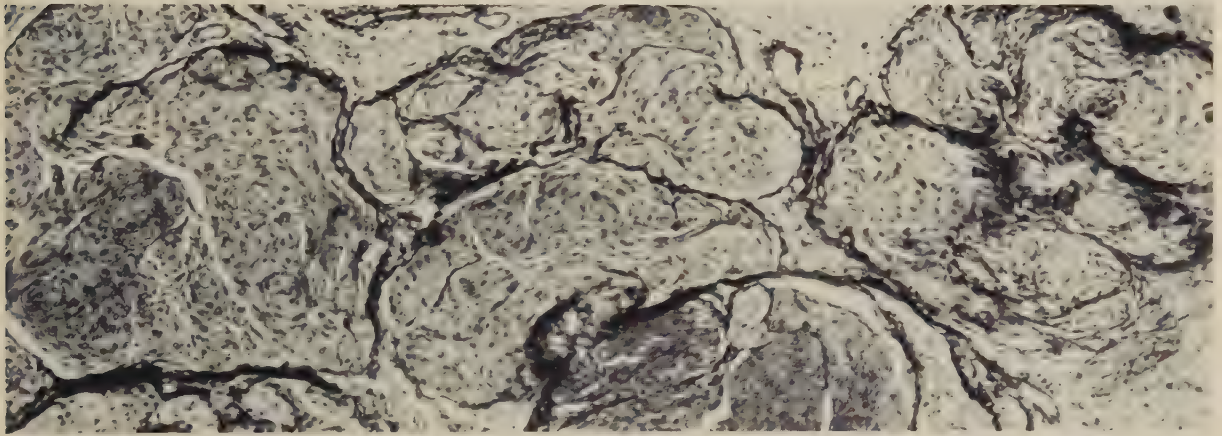
D. The large and multinucleated acidophilic cells are gemistocytic astrocytes. x 145.



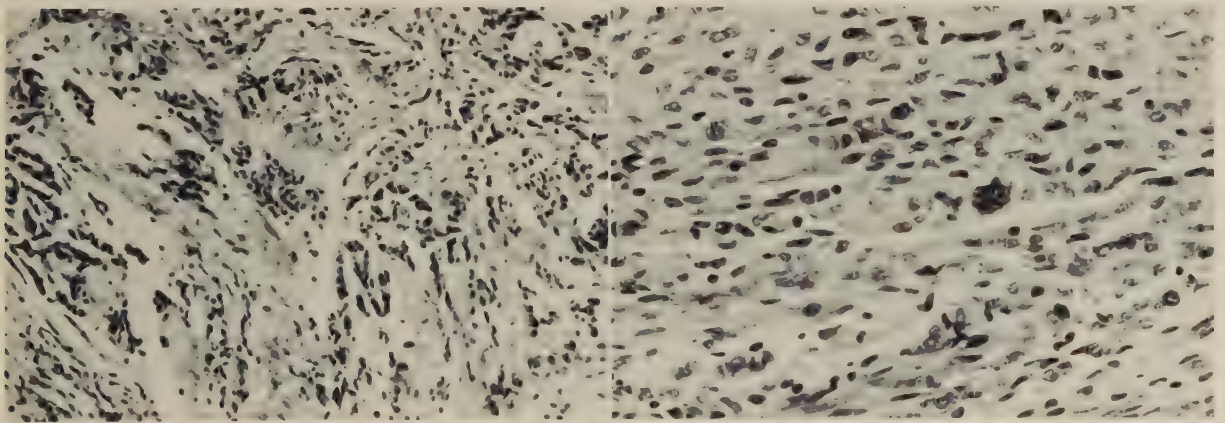
Astrocytoma, nose, reported as a ganglioneuroma, had not recurred 11 years after removal. Gemistocytic astrocytes predominate. Note isolated spicule of bone. x 55, x 235.



Polypoid mass in left superior meatus, 5 years after removal of intracranial meningioma from olfactory groove of a 33 year old Negro man. This is the meningothelial type, but the cells are smaller than usual. x 48, x 185. (J. R. Kriz, V.A.H., Richmond, Va.)



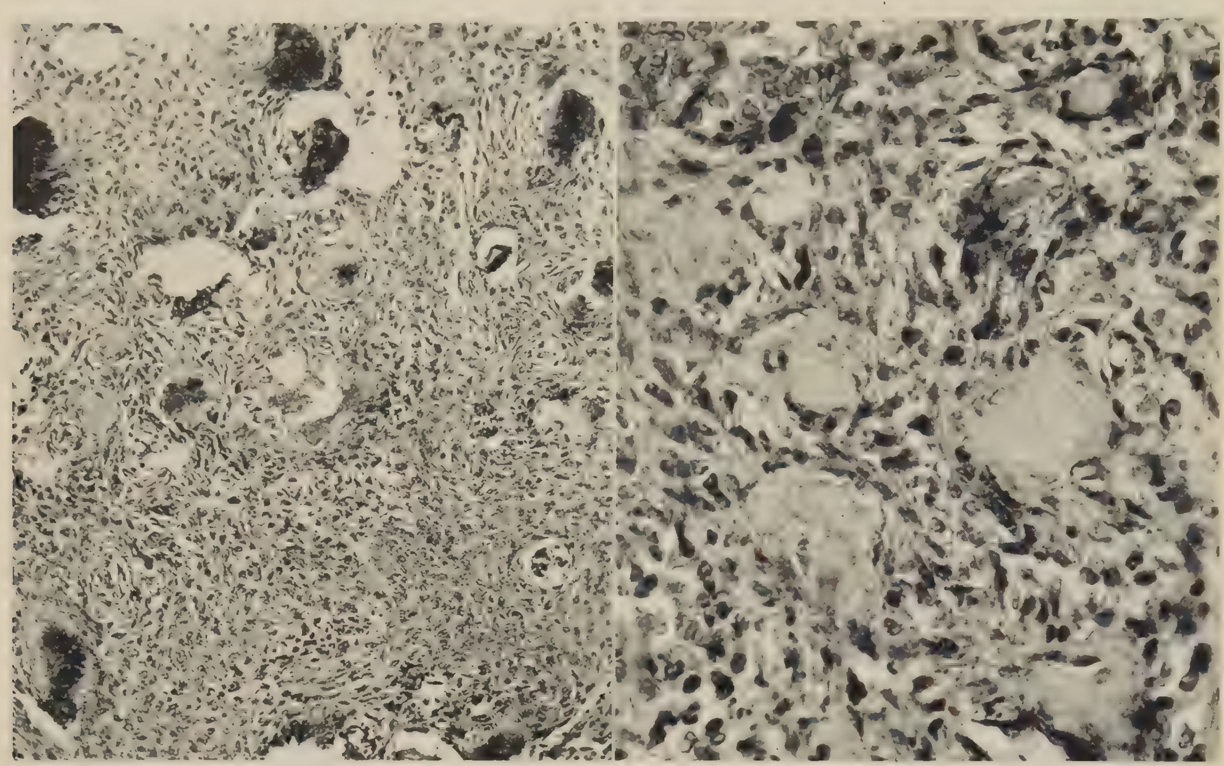
Polypoid mass, from upper nasal cavity of a 49 year old woman, is a more typical meningothelial tumor with robust epithelioid cells arranged in whorls. x 110. Five years previously a meningioma had been removed from the anterior cranial fossa. Frontal and ethmoidal sinuses and orbit were eroded.



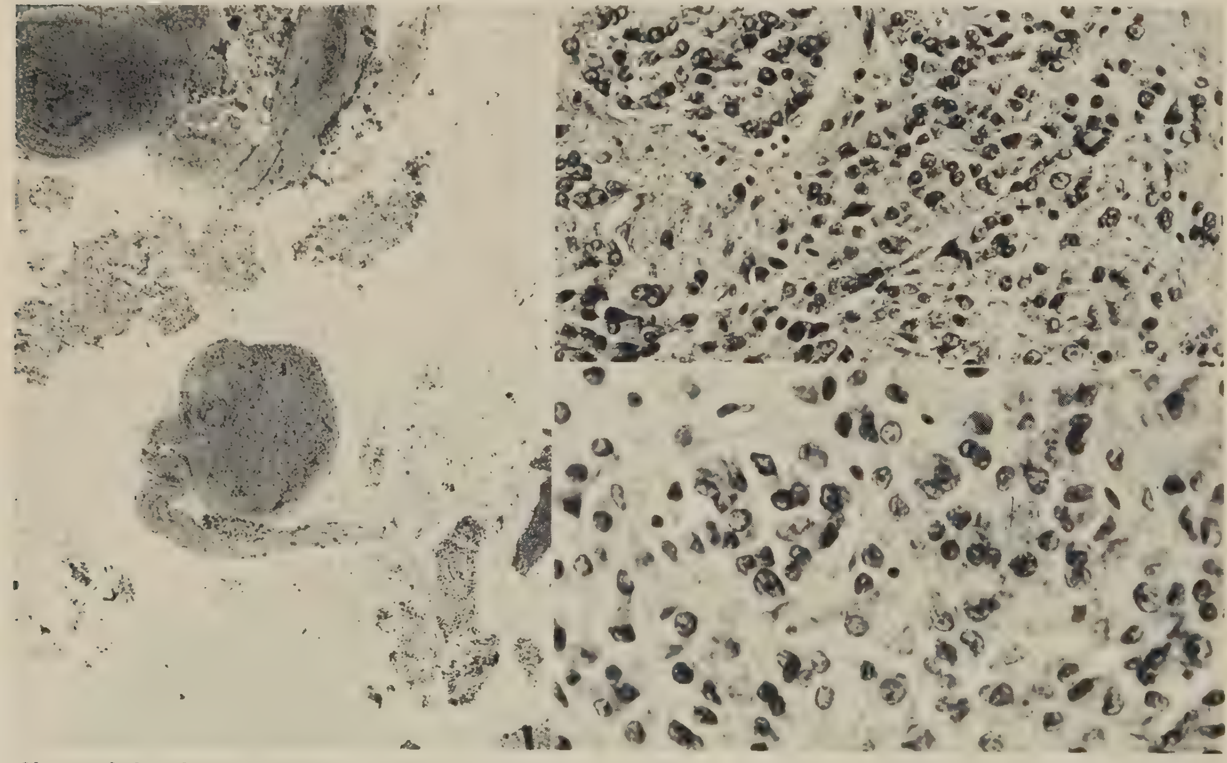
Meningioma, left anterior cranial fossa, generally of epithelioid type with more than usual pleomorphism, in a 58 year old colored man. Headache and mental symptoms had been present for many years and epistaxis for few weeks before death. Tumor involved left orbit, ethmoidal and sphenoidal sinuses and superior nasal cavity. x 90, x 250.

MENINGIOMA, FRONTAL SINUS

CHROMAPHOBE ADENOMA OF PITUITARY AND SPHENOIDAL SINUS



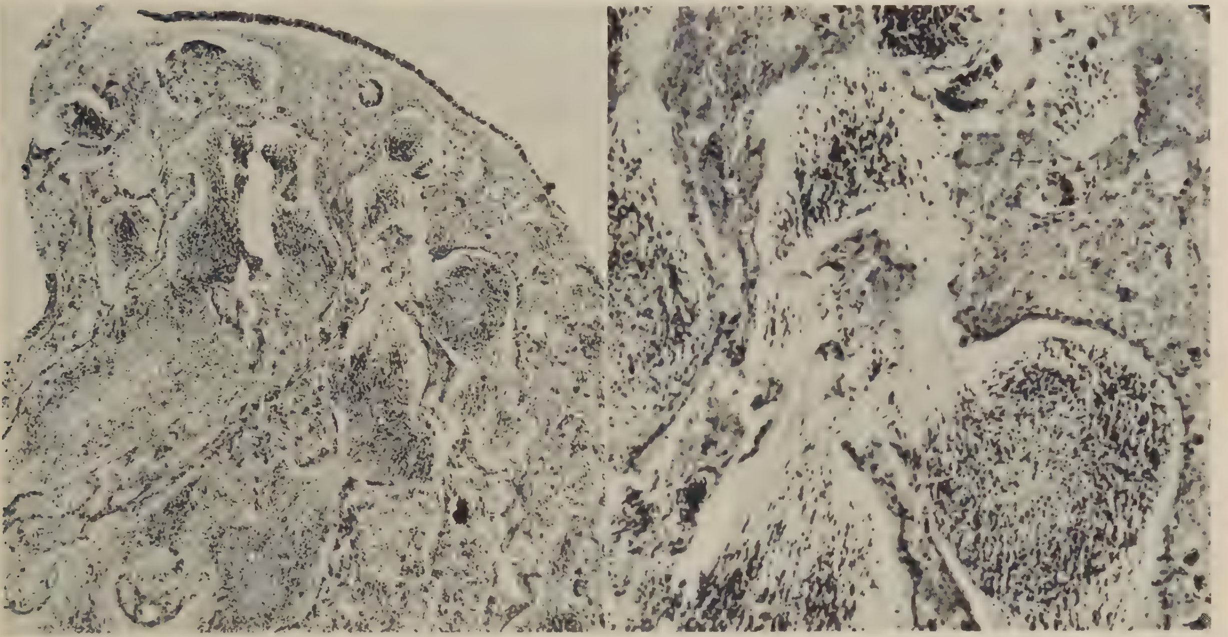
Psammomatous meningioma, from right fronto-ethmoidal region of a 12 year old Korean. Cells of a more fibrous type, with numerous hyaline and calcified bodies. x 125, x 390. The tumor was present for 5 years and invaded orbit, frontal and ethmoidal sinuses and posterior wing of sphenoid.



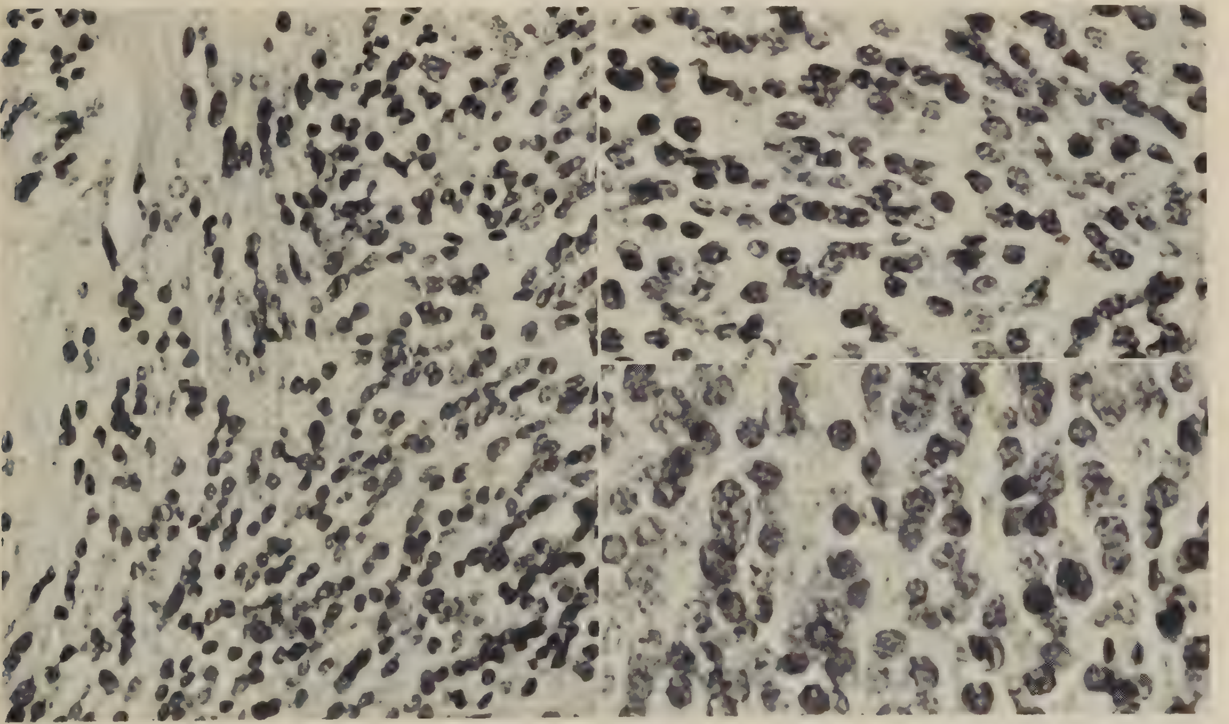
Chromaphobe adenoma, pituitary, in 37 year old colored man with an 8 year history of bitemporal hemianopsia and x-ray evidence of tumor in pituitary area. Aspiration biopsy from the sphenoidal extension demonstrates cells that are somewhat pleomorphic but of pituitary pale cell type. x 24, x 260, x 395.

OLFACTORY (?) NEUROBLASTOMA

OLFACTORY NEUROEPITHELIOMA; (L'ESTHESIONEUROCYTOME OLFACTIF L'ESTHESIONEUROBLASTOME OLFACTIF)



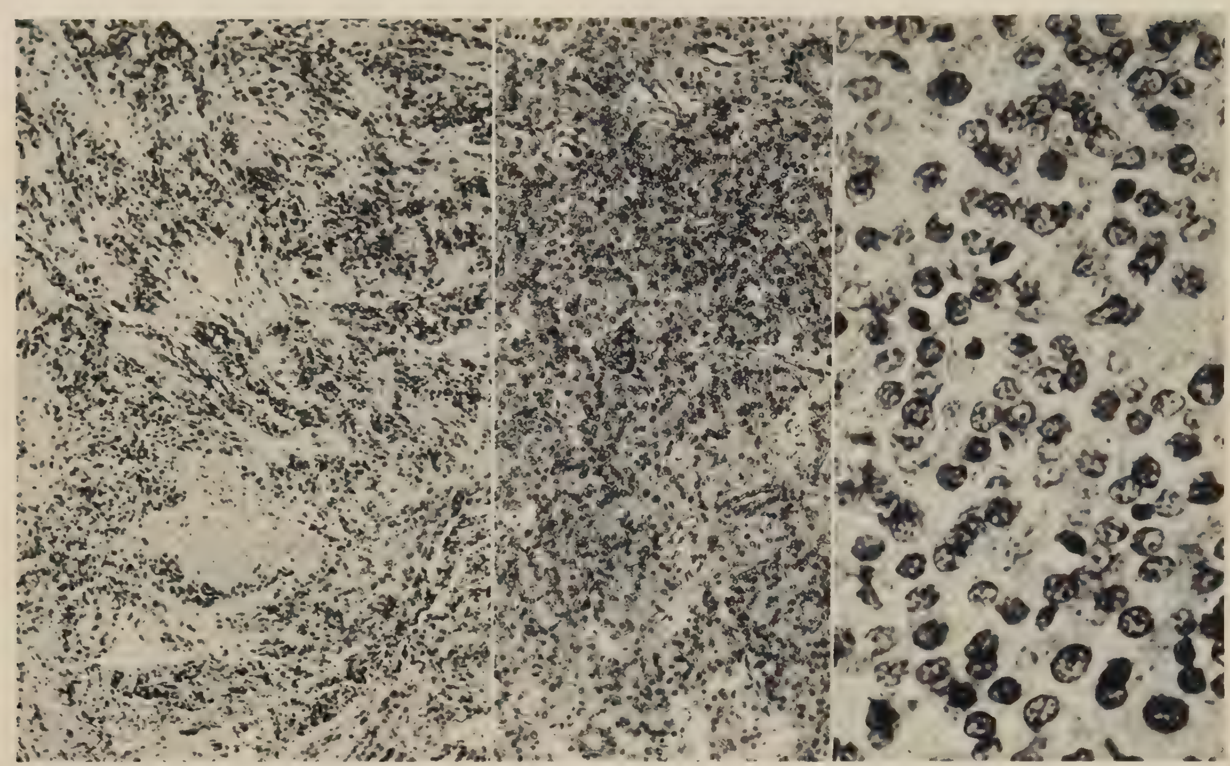
Olfactory neuroepithelioma (Stout). Polypoid tumor of roof of nasal cavity in an adult male. x 35, x 100. (Slide contributed by Dr. A. P. Stout. Case used in Atlas of Tumor Pathology, Section II, Fascicle 6, Tumor of Peripheral Nerves, Washington, D.C., AFIP, 1949.) Berger, Luc, and Richard (1924) first described a tumor ("l'esthesioneuroepitheliome olfactif") which, they believed, arose from esthesioneuroblasts" of olfactory placode origin, with features of both central and sympathetic "neuroepitheliomas."



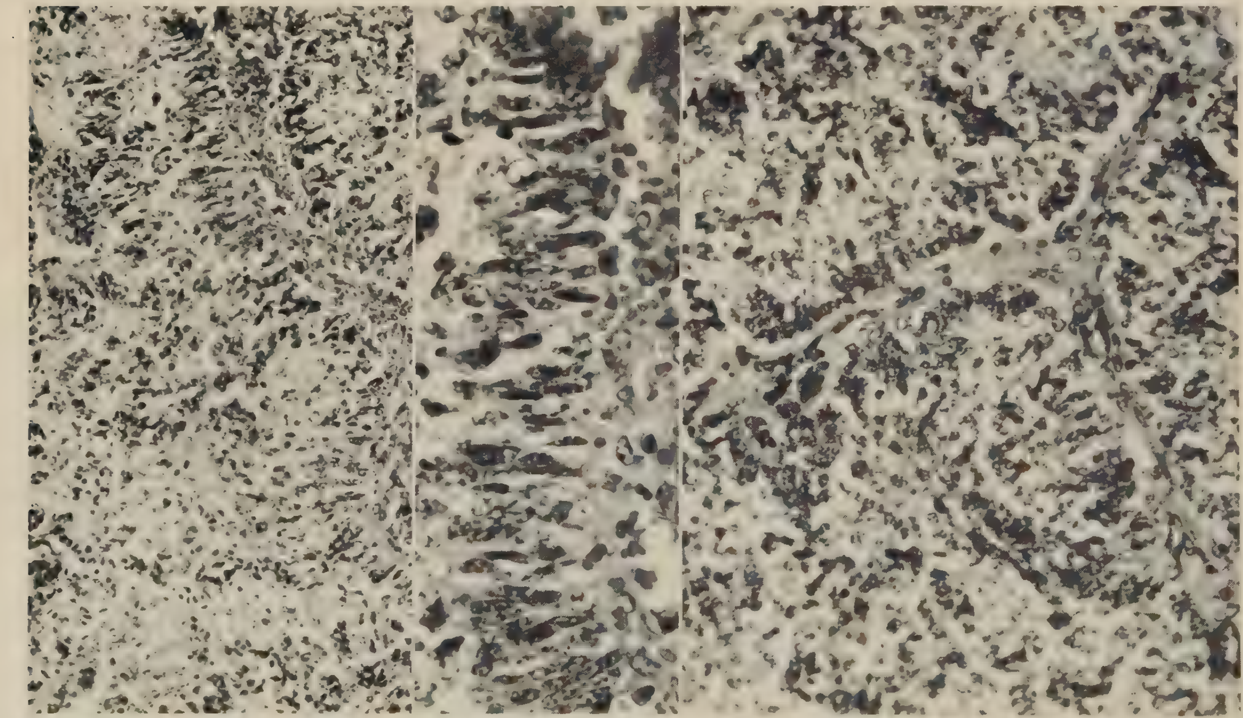
Confluent or intertwining irregular masses of cells with scant cytoplasm and uniform nuclei containing evenly dispersed chromatin, in a delicate, oriented fibrillar network, prominent in relatively anuclear zones. x 315, x 475, x 600. Berger and Coutard (1926) termed an identical tumor "l'esthesioneurocytome olfactif," believing it a neoplasm showing differentiation only in direction of neurocytes and neurofibrils. Other authors have suggested origin from sympathetic elements in the nasal mucosa.

OLFACTORY (?) NEUROBLASTOMA

PRIMARY INTRANASAL NEUROBLASTOMA



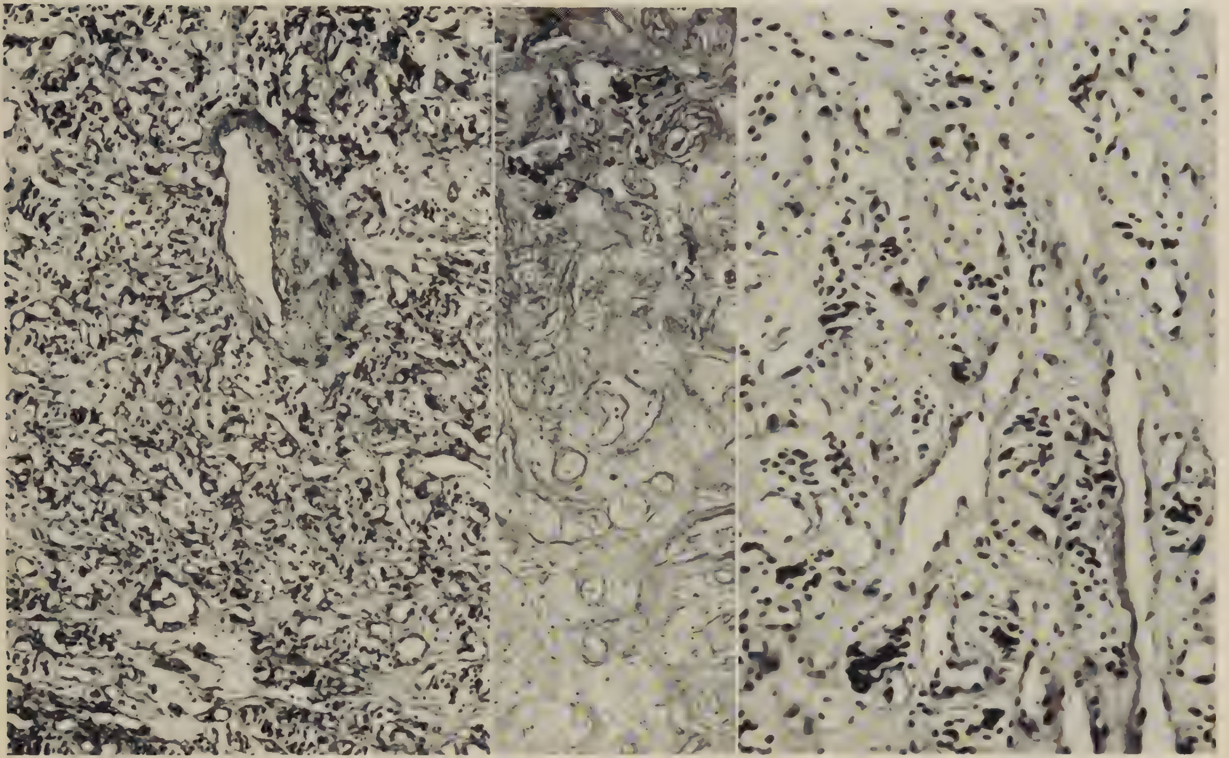
Primary intranasal neuroblastoma, blocking right nostril of a 57 year old female. Portions of this tumor were similar to fields on preceding plate. x 90, x 135, x 650. One of three similar tumors in adult females reported by Schall and Lineback (1951), who found 14 other cases in the literature including the French authors cited in the previous plate. x 90, x 135, x 650.



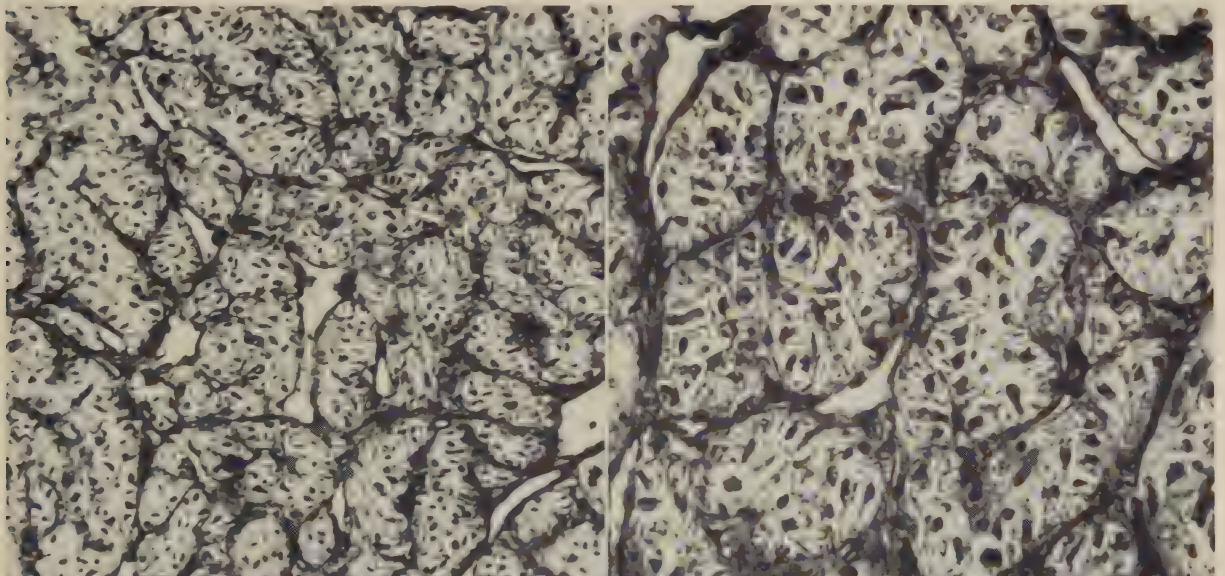
More undifferentiated neuroblastoma clinically evident in a 36 year old man for several months, filled the right nasal cavity, ethmoids and antrum. Masses of undifferentiated fairly uniform rounded cells (left x 90), with occasional zone of palisaded elongated cells (center x 450), and rosette-like clusters (right x 185).

NON-CHROMAFFIN PARAGANGLIOMA, NASOPHARYNX

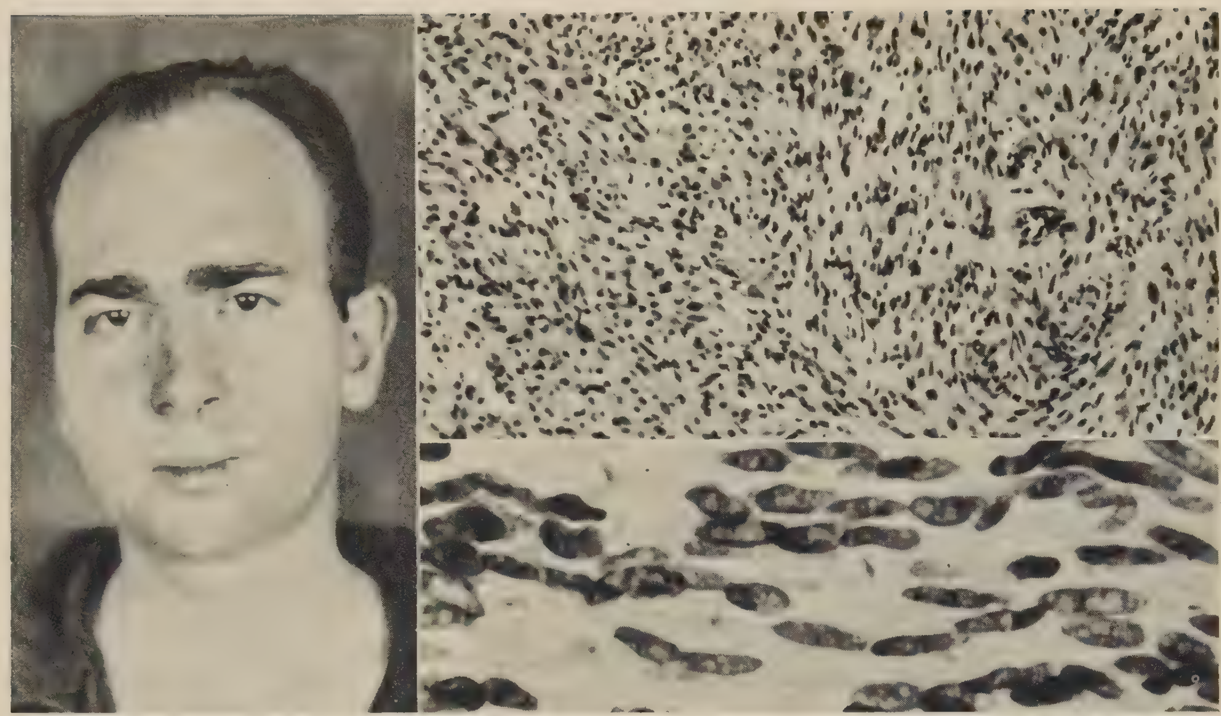
GLOMUS JUGULARE



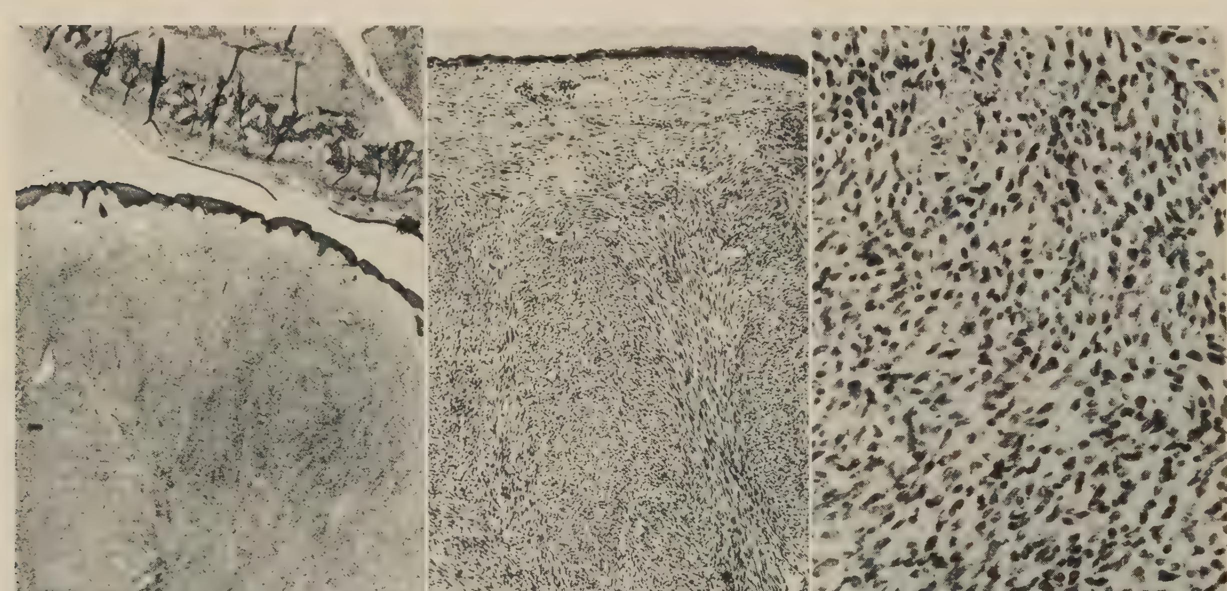
Non-chromaffin paraganglioma primary in temporal bone (glomus jugulare), extending into and filling nasopharynx of a 54 year old woman. No metastasis. Organoid collections of poorly defined cells associated with rich vascularity. x 100, x 90, x 160.



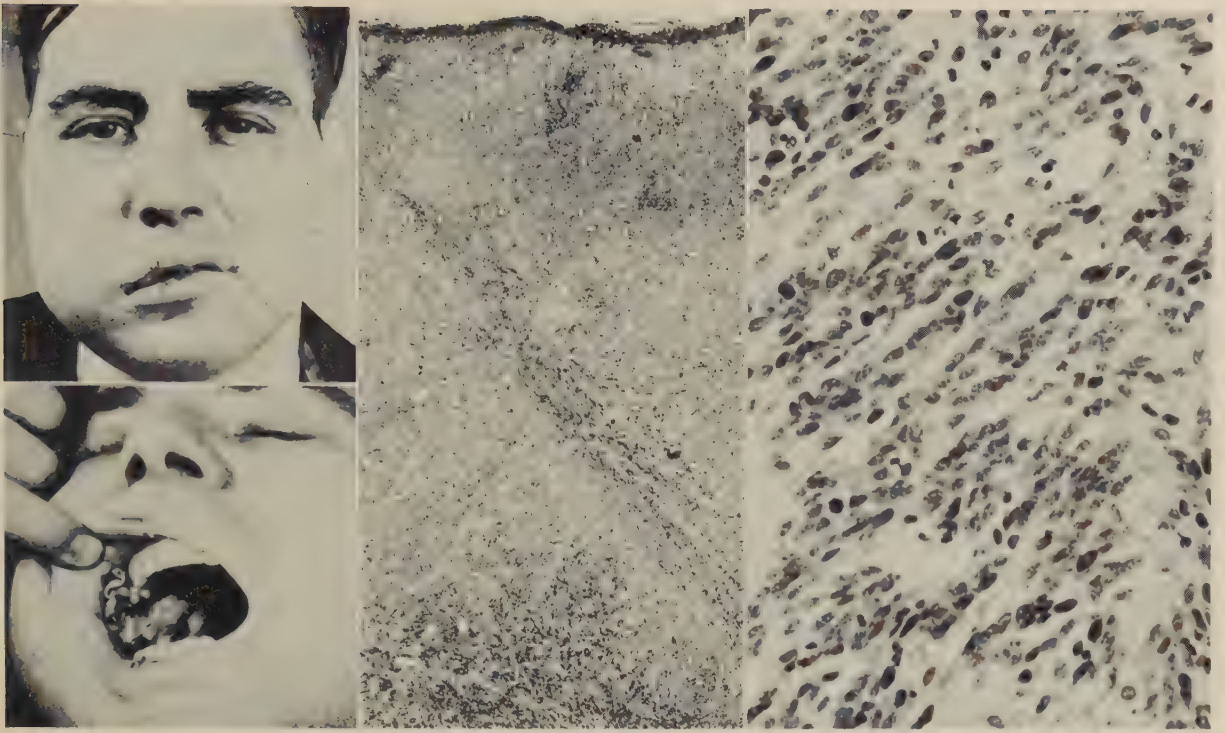
Organoid cellular pattern and vascularity suggest paraganglioma. This tumor has also been called malignant giant paraganglioma, alveolar soft tissue sarcoma, and malignant myoblastoma. x 145, x 315.



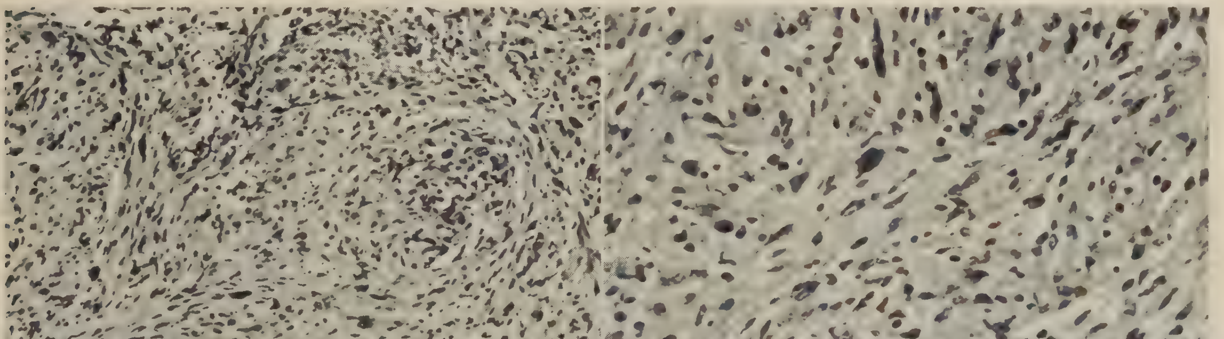
Fibrosarcoma, filling right maxillary sinus of 28 year old man with painless swelling of right side of face of two months' duration. Roentgenographic evidence of destruction of lateral wall of right maxillary sinus. Moderately cellular, well differentiated tumor composed of interlacing bundles of fibroblastic cells and fibers. Cells are fairly uniform in size and shape. Suggestive palisading of nuclei in focal areas. x235. Spindle-shaped, hyperchromatic nuclei, but only rare mitosis in cellular area. About x900.



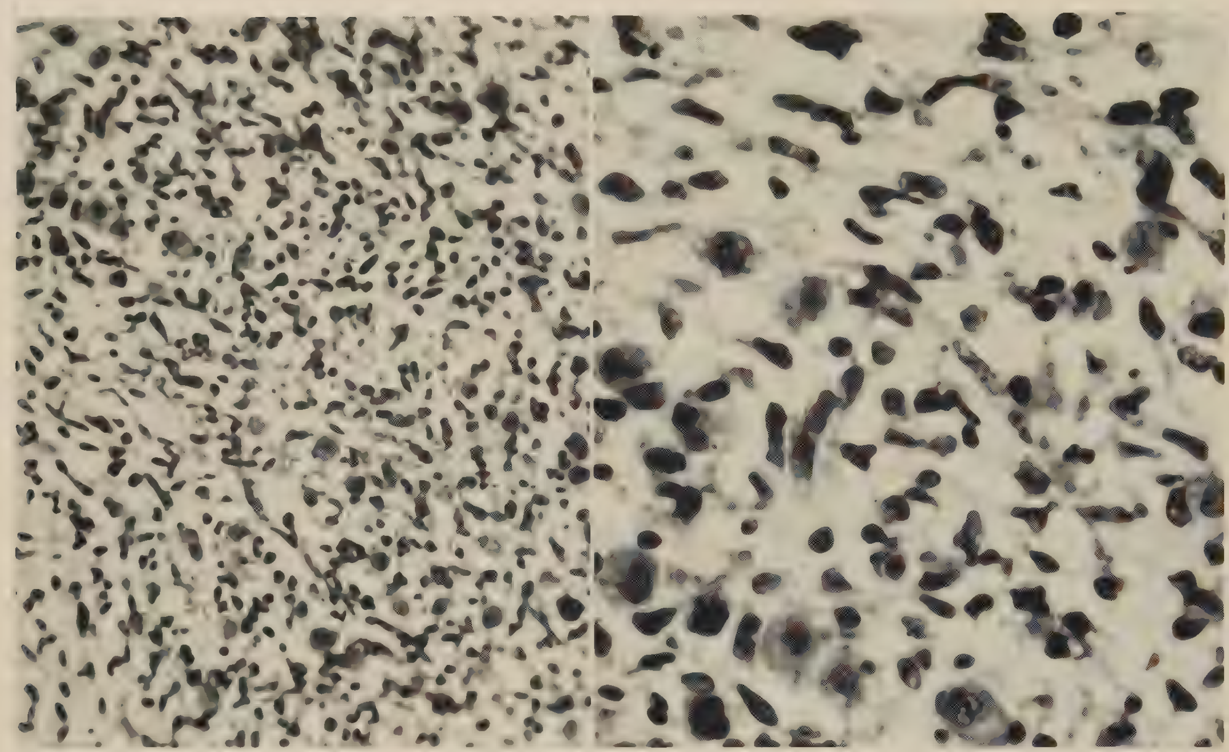
Fibrosarcoma, right frontal sinus in 39 year old woman with intermittent bleeding from right nostril. Swelling and pain in right orbital region for two weeks; roentgenographic evidence of destruction of floor of sinus. **A.** Biopsy from extension to middle turbinate. Bulky cellular mass. Squamous metaplasia of surface epithelium. x14. **B.** Intertwining fascicles of very cellular tumor; numerous thin-walled vessels. x76. **C.** Hyperchromatic nuclei; relatively frequent mitoses. x285.



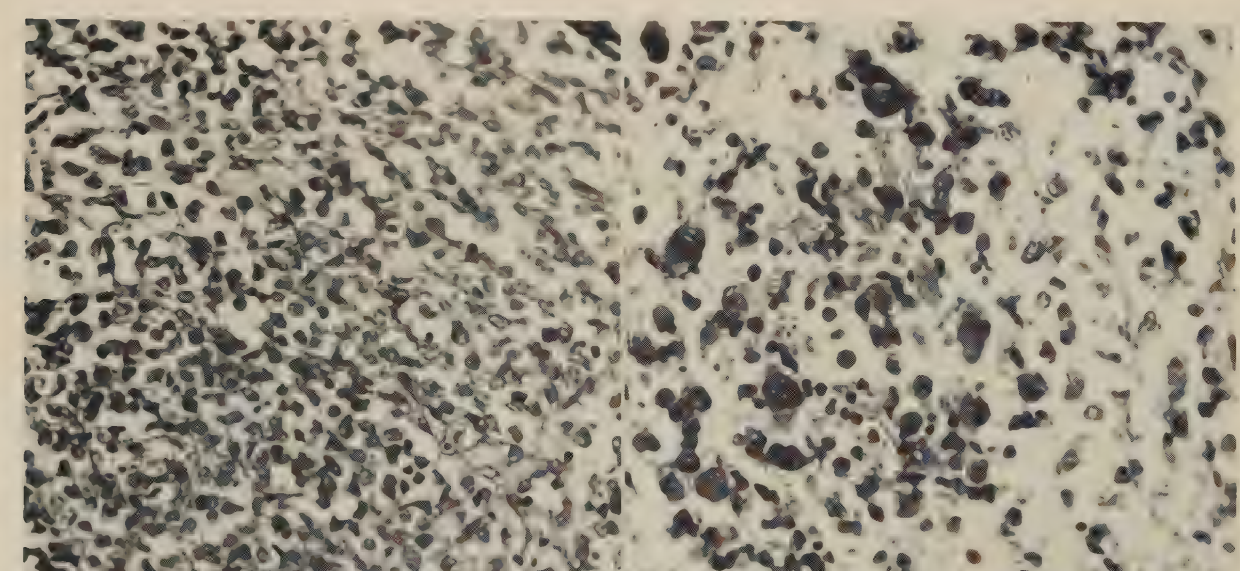
Fibrosarcoma, primary in maxillary sinus of a 27 year old man, caused progressive swelling of right cheek and eroded through alveolar process. Fungating growth rapidly extended through alveolus into oral cavity after extraction of a molar tooth. Death nine months after extraction was attributable to tumor extension with invasion of the base of the skull and brain abscess. Very cellular tumor with partly whorled pattern and palisading of nuclei suggesting neurogenous origin. Very frequent mitoses. x20, x315.



Sarcoma of maxillary sinus, radically resected from a 26 year old woman after six months' treatment for sinusitis. It had grown rapidly, eroding into the orbit, causing proptosis, and invading the lateral nasal wall. *Left:* whorled pattern suggestive of smooth muscle origin, but it is probably a rapidly growing fibrosarcoma. x125. *Right:* mitoses and moderate pleomorphism with occasional large bizarre and giant forms (a feature more characteristic of myosarcoma and liposarcoma). x275.

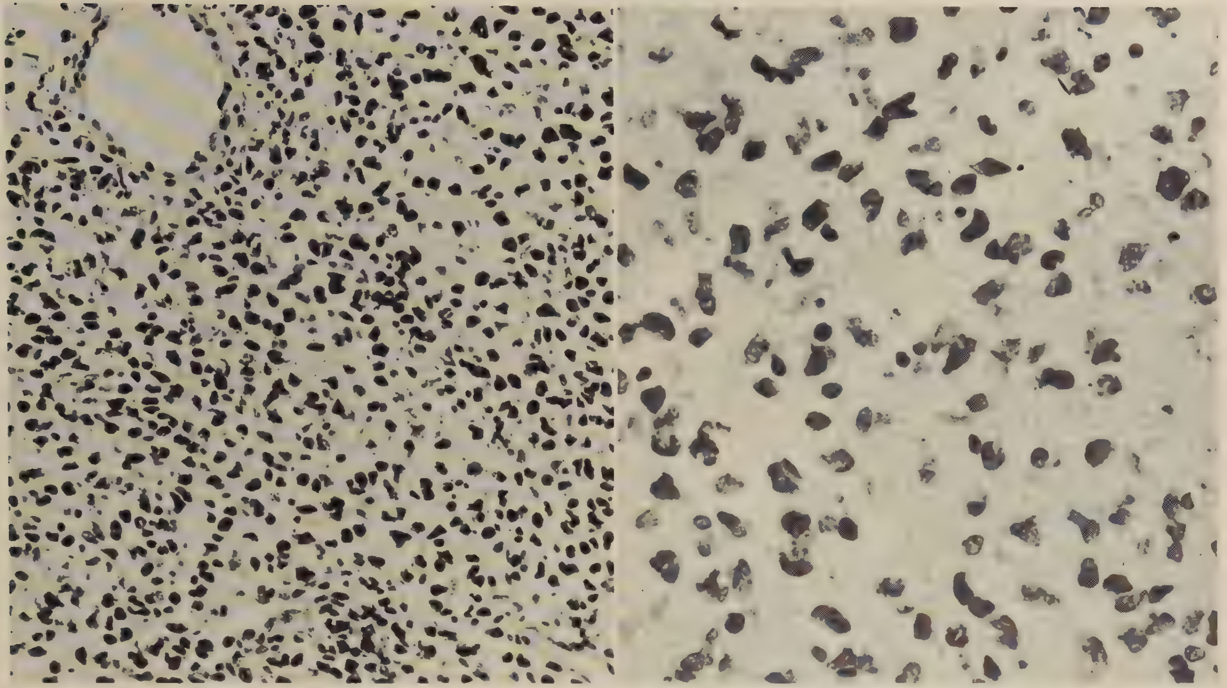


Embryonal rhabdomyosarcoma in a 6 year old girl, presenting as in right nasal cavity, an extensive tumor displacing the septum. Partially necrotic mass in nasopharynx; soft and hard palates depressed. Nasal tumor composed predominantly of small, oval and spindle cells with moderate numbers of larger rounded, polyhedral or irregular cells with distinctly acidophilic cytoplasm. x275, x500. (J.F. Beauregard, F.E. Sherman, Pittsburgh.)

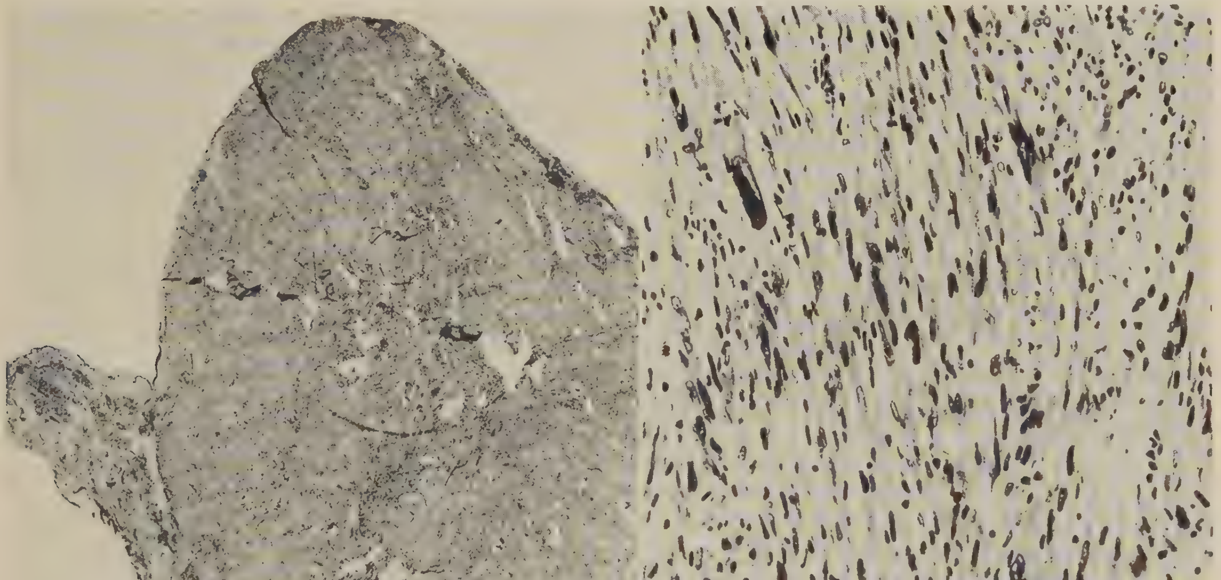


Completely undifferentiated groupings of uniform round cells with scant cytoplasm and vesicular nuclei *(left)* were present in another tumor, removed from nasal cavity of 9 month old baby. Focal areas *(right)* contained large, occasionally bizarre and giant cell forms with irregular hyperchromatic nuclei and intensely eosinophilic cytoplasm or coarse processes. Both x395. (R.A. Yourd, Iowa City.)

RHABDOMYOSARCOMA



Embryonal rhabdomyosarcoma, an extensive mass in the nasopharynx of a 7 year old boy who died with metastases to cervical, mesenteric and paravertebral nodes, lungs, mediastinum, liver, vertebrae and skull; and local extension to frontal and ethmoid sinuses and left petrous bone. Myxomatous character of widely spaced cells of varying size and shape is suggestive of sarcoma botryoides of genitourinary tract. x210, x490.



Sarcoma, probably rhabdomyosarcoma, involving entire inferior turbinate of a 49 year old man, producing nasal obstruction and discharge. Polypoid cellular neoplasm infiltrating normal structures of adjacent mucosa *(left)*. x8. Numerous mitoses and bizarre, giant and multinucleated cells, including strap-shaped and racquet-shaped forms, but no distinct striations. x160. (Both cases from J. Kirchner, New Haven, Conn.)

CHAPTER 19

PHARYNX

The pharynx is divided into three portions: the upper or nasopharynx, which extends down to the level of the soft palate; the middle portion or oropharynx, which extends down to the level of the hyoid bone, and the lower third, the hypopharynx or laryngopharynx which extends down to the lower border of the cricoid cartilage.

The **nasopharynx** is a continuation of the nasal portion of the respiratory tract and is covered, therefore, with respiratory epithelium. Its mucosa differs from that of the nose by the presence of large amounts of lymphoid elements just beneath the epithelium. These lymphoid elements are particularly prominent in the fossa of Rosenmüller and in the upper posterior wall where they constitute the clinical adenoids, the pharyngeal or Luschka's tonsil. Here they are congregated about a sinus-like depression in the mucosa, which normally ends very close to the bony wall of the pharynx. This structure is lined by respiratory epithelium and is called the pharyngeal bursa. In addition to this depression there are clefts between the lobules of lymphatic tissue, but they are not as deep or as sacculated as are those in the faucial tonsils. The lymphoid masses have germinal centers and a supporting framework of connective tissue septa. It is in the adenoid that the close relationship between the epithelium and the lymphatic tissue can best be seen. This is the histologic entity lymphoepithelium. The epithelium that dips into the crypts is usually of the respiratory type, but there may be areas of squamous cells, particularly in the lower portion of the adenoids and also in areas over the surface if the adenoids have been the seat of chronic inflammation.

There are numerous seromucous glands in the pharyngeal mucosa, particularly abundant in the fossa of Rosenmüller, the orifices of the eustachian tube, and the septa of the adenoids.

The roof of the pharynx is composed of fairly dense stroma which contains a great number of mucous glands and is attached to the sphenoid bone. Deep in the mucosa of the roof is the pharyngeal pituitary. The amount and character of its elements differ in individuals, from groups of chromaffin epithelium to acinar structures containing colloid material. Only the elements of the anterior lobe of the pituitary are found in this location. These are the remains of Rathke's pouch persisting along the line of the invagination of the pharyngeal mucosa into the cranial cavity to form the anterior lobe of the pituitary. It is claimed this ectopic element is sometimes functional.

The posterior bony wall of the nasopharynx is formed by a continuation of the basilar process of the occipital bone and by the cervical vertebrae. Lateral pockets starting at the upper posterior corners of the nasopharynx extend upward and backward along the posterior walls of the eustachian cartilages for a considerable distance—from 0.7 cm. in depth, in children to 1.3 in adults. The lymphoid tissue surrounding the pockets extends an additional centimeter beyond them. These are the fossae of Rosenmüller or pharyngeal recesses.

The **mesopharynx (oropharynx)** is bounded posteriorly by the first and second cervical vertebrae and anteriorly by the soft palate and the faucial tonsils, and its orifice is defined below and anteriorly by the lingual tonsil that is embedded in the base of the tongue. The stroma of the mucosa consists of loose areolar tissue supported by a rather dense network of elastic fibers. This is further supported by a muscular wall, especially laterally by the salpingopharyngeal muscles. The elastic meshwork is intimately connected with the aponeurosis of these muscles and posteriorly, where they are absent, with the periosteum of the bones. Nerves, blood vessels and lymphatics are abundant in the submucosa throughout the pharynx, and mucous glands are present in the mesopharynx.

The epithelial mucosa is of the squamous type except on the upper nasopharyngeal side of the soft palate where it is respiratory epithelium. There is a small amount of lymphatic tissue in the mesopharyngeal mucosa, but it is not as abundant or as well organized as in the nasopharynx.

Hypertrophic changes in the cervical vertebrae may cause bulging of the mucosa over the posterior wall that simulates a retropharyngeal infection.

Hypopharynx.—In the posterior portion where the pharynx is continuous with the esophagus, the mucosa is very thin and forms a spot vulnerable to trauma. This thin mucosa covers a loose areolar tissue in which infection can spread rapidly. The squamous type of epithelium continues into the hypopharynx and covers, therefore, the laryngeal surface of the epiglottis, the edges of the true cords, and the anterior surface of the arytenoid cartilages.

The student is referred to Woodson's detailed review of the anatomy and embryology of these parts. It is of great practical importance that the otolaryngologist be familiar with the fascial and muscular planes and the lymphatics of the pharynx because of their bearing on the extension of infections.

PHARYNGITIS

Acute pharyngitis is not confined to any one structure. The infection may begin in the crypts of the tonsils, the recesses of the adenoids, in the nasopharynx, the fossae of Rosenmüller, the lateral folds, or the lingual tonsil. It is usually accompanied by rhinitis, but the process may be limited to the pharynx or it may be the initial site of a "cold." The pathologic picture in this stage is simply that of a catarrhal inflammation, i.e., congestion, edema, serous or mucous exudate. When it is a bacterial infection, particularly by one of the streptococci, the reaction is more intense and there may be flakes of white pseudomembrane over the surface of the mucosa and especially over the orifices of the crypts of the tonsillar tissue. A common complication is edema of the uvula. Streptococcal infections, especially hemolytic forms, are of particular importance because of the possible complications. The most serious complications are pneumonia, acute otitis media, septicemia, bacteremia, and pharyngeal abscesses and cellulitis.

Microscopically, the characteristic changes are loss of epithelium, emigration of polymorphonuclear leukocytes, edema of the submucosa, mitosis and phagocytosis in the germinal centers of the lymph follicles, and congestion of the blood vessels.

Chronic pharyngitis is usual among those who suffer from infections of the upper respiratory tract or from allergies. Enlargement of the lymphatic tissue elements in the pharynx is a common manifestation. Smoking and the drying effect of inadequately warmed and humidified air add to the difficulty. The chief clinical symptom is "sore throat."

Woodson emphasized the clinical importance of the large lateral bands which lie behind the tonsillar pillars as an indication of chronic inflammation of the nasopharynx. They seem to suggest a systemic rather than a predominantly local cause, including an allergic or a psychosomatic factor. These beefy red bands extend up into the fossae of Rosenmüller.

The chief objective feature of chronic pharyngitis is hyperplasia of the lymphoid elements, especially those on the posterior pharyngeal wall, with accompanying moderate hyperemia. In addition to the "granulations," white spots are evident, representing either the plugged orifices of the mucous glands or hyperplastic lymph follicles with large germinal centers rich in phagocytosing reticuloendothelial cells. These enlarged germinal centers look like minute sterile abscesses.

Microscopically, varying amounts of chronic cellular exudate are accompanied by an increase in connective tissue and reticular elements, sometimes to the extent that there is recognizable scarring. The glands of the mucosa usually show increased secretory activity, and the orifices may be compromised by the hyperplasia of the surrounding lymphatic follicles and be plugged with desiccated mucus and debris.

Follicular pharyngitis, really a form of chronic pharyngitis, is more common in young allergic individuals and is associated with hyperplasia of the lymphoid tissue elements in this area. This hyperplasia involves also the tonsillar tissue, when present, and the adenoids. The lymph follicles appear clinically as whitish nodules in sharp contrast to the reddened mucosa of the oropharynx. During acute exacerbations the nodules become bright red and swollen.

Mesopharyngitis proliferans is a condition of early middle life manifested clinically by an acute febrile reaction and severe pain in the throat. The mucosa is criss-crossed by large dry white bands with dark red granulations between them. The bands are scar tissue, residua of former infections or the result of therapeutic cauterization. The exacerbation may be complicated by pneumonia, otitis media, or pharyngomaxillary abscess.

When ozena extends to the pharynx, the mucosa is pale, parchment dry, and crusted.

Keratosis pharyngeus (pharyngitis sicca) appears clinically as white spots firmly attached, particularly over the orifices of the crypts of the tonsils and pharynx. These spots are elevated and rounded and resemble particles of raw tapioca. The white spots may be found also on the epiglottis and in the larynx. There is practically no inflammatory reaction about them. The patient usually complains only of mild pharyngitis. When the condition is limited to the tonsils it must be differentiated from follicular tonsillitis, and when the pharynx is involved, from granular pharyngitis. It is said that this condition does not occur in the mucosa where there is no lymphoid tissue, but it is clinically certain that it does occur in the larynx. The commonest sites are the faucial and lingual tonsils.

Microscopically, these white nodules are made up of masses of squamous epithelium the seat of marked hyperkeratosis evidenced by the piling up of keratin flakes. Even microscopically there is a paucity of inflammatory reaction.

Practically always associated with this process are the mycelia of fungi, the most common being leptothrix. This is so common an association that the disease has been called leptothrixal or mycotic keratosis. Beck claimed, however, that the condition may occur without the fungi in persons who use tobacco. The etiology is obscure, but the hyperkeratosis can be due to a low grade chronic irritation of the involved squamous epithelium or even to vitamin deficiency, especially of A.

Fusospirochetal Pharyngitis. — Vincent's angina, stomatitis, trench mouth are synonyms for the fusospirochetal infection which produces gray ulceromembranous lesions, causing much destruction, usually of the tonsil or gingivae.

The fusiform bacillus stains readily and is gram-positive. The spirochete is delicate and irregular, stains poorly, and is gram-negative. Their presence in a smear is not diagnostic, but when the two organisms occur in enormous numbers in an affected area, they are probably the exciting factors. They are anaerobic organisms, and therefore are most abundant in the deeper layers of the lesions.

Ulceration and necrosis are associated with the formation of a fibrinous membrane containing many polymorphonuclear cells, with a zone of leukocytic demarcation. If chronic ulcers remain in the tonsil crypts the patient becomes a carrier.

"Adenoids."—Hyperplasia of the adenoid tissue is so common in children that it is almost physiologic. It is really not uncommon in adults. A seemingly small adenoid can produce serious results, particularly in a child with a shallow pharynx. In adults it interferes little with respiration, but in both children and adults it can contribute to the chronicity of infections of the middle ear, nose, paranasal sinuses, and even of the lower respiratory tract.

The hyperplastic adenoid appears on direct examination as a lobulated pink mass on the posterior pharyngeal wall behind the soft palate. In adults particularly, enlargement of the adenoid necessitates the differentiation of simple hyperplasia from a tumor of lymphatic tissue. Lymphosarcoma is rapidly growing and results in a soft, red, ulcerating tumor. In leukemia, the blood picture will be diagnostic.

In children, hyperplastic adenoids may be manifested clinically by mouth breathing, nasal speech, and the adenoid facies of pinched nose and narrow nares. The adenoid tissue usually increases in bulk following tonsillectomy in children, especially in those suffering from allergy.

On microscopic examination of adenoid tissue it is evident that the enlargement is not due so much to an increase in the number of lymphocytes as to the increase in number and size of the follicles. In addition, however, the tumefaction is accentuated by edema, exudate, and the accumulation of cells and debris in the crypts. The respiratory epithelium may undergo metaplasia to the squamous type. That lining the crypts becomes edematous and infiltrated by cells of the exudate, so that it is difficult to recognize. Following episodes of suppuration there may be scarring.

Tornwaldt's Syndrome.—The significance of the pharyngeal bursa was first emphasized by Tornwaldt in 1885. He described the consequences of obstruction to the orifice of the bursa caused by infection as an accumulation either of exudate in the dilated bursa or of secretion resulting in cyst formation. It is usually associated with frequent upper respiratory infections.

The pharyngeal bursa was first described in man by Mayer in 1842. Luschka gave a more complete and accurate description in 1868. He believed it to be a persistence of the oral-hypophysial duct. The most recent comprehensive study was made by Snook in 1934. He found a bursa in 40 per cent of the embryos studied. The notochord is in contact with the lining epithelium of the nasopharynx, and as the former degenerates, the epithelium follows along the tract toward the posterior bony wall of the pharynx. The subsequent development of lymphoid tissue about this epithelium-lined tract emphasizes the depression that appears in its adult state.

The intimate relationship between the cells of the adenoid tissue and the epithelium is characteristic of lymphoepithelium. The occlusion of the orifice of the bursa is probably most commonly caused by hyperplasia of the surrounding adenoid elements. The bursa may remain cystic with accumulation of cellular debris and secretion from the glandular epithelium, or it may become infected and result in Tornwaldt's abscess. A similar but smaller lesion follows occlusion of other clefts of the adenoids. To eradicate the Tornwaldt lesion it is necessary to excise the epithelial lining down to the periosteum of the sphenoid.

Microscopically, the respiratory epithelium that normally lines the bursa may in part have undergone metaplasia to squamous type, or, in the presence of infection, it may be absent. Surrounding the base are abundant lymphatic tissue elements with germinal centers, but these may be obscured by exudate, usually of lymphocytic and plasma-cell type, although polymorphonuclear leukocytes will be included if there is active infection. The contents of the cysts vary. In the absence of infection there will be epithelial debris, the pyknotic nuclei of escaped small mononuclear cells, and cholesterol crystals. In the presence of bacterial infection there is purulent exudate to form the Tornwaldt abscess.

Retropharyngeal abscess results from (1) pyogenic infection of the lymphatic tissue elements in the mucosa, causing deep suppurative necrosis with spread of the infection into the prevertebral cellular tissue; (2) extension of peritonsillar abscess or cellulitis that may be bilateral; (3) release of the contents of an abscess of the pharyngeal bursa into the prevertebral tissues; (4) extension of infection from suppurative osteomyelitis of the petrous portion of the temporal bone, of the sphenoid, and rarely of the cervical vertebrae. Amplification of this subject will be found in the discussion of deep infections in the section on the neck.

Diphtheria is an acute infectious disease caused by the *Corynebacterium diphtheriae,* the Klebs-Loeffler bacillus of older nomenclature. It is an example of the group of infections in which the bacteria localize and produce an exotoxin that is responsible for serious systemic reactions. The infection is further characterized as the type causing the diphtheritic, croupous, or pseudomembranous inflammation.

The epidemiology depends on the carrier, and the individual case is the result of direct infection from one human being to another, although the organism can remain viable for a few days in a free state. The infection can also be transmitted by household pets, especially the cat. The carrier presents a problem to the otolaryngologist. The most frequent sites of the organism in carriers are the tonsils and nose. When the nose is implicated, the carrier is usually the victim of chronic diphtheritic rhinitis.

The disease is chiefly one of childhood, including infancy. It usually manifests itself in the fauces with severe edema and congestion, followed by development of grayish patches of membrane that are characteristically adherent. From the fauces it spreads to the upper and lower portions of the respiratory tract to varying degrees. Cervical lymphadenitis is usually an accompanying feature.

The pathologic changes occur rapidly with the outpouring of exudate rich in fibrin in which are enmeshed many polymorphonuclear leukocytes and much nuclear debris. The surface epithelium disappears, but there is an inseparable continuity between the false membrane and the subepithelial stroma which is also involved in the exudative process.

Histologically, the membrane is roughly in three layers: the outer zone of necrosis in which the cell outlines are lost and only the nuclear remains are seen enmeshed in hyalinized strands of fibrin. The next layer is made up of exudate composed of polymorphonuclear leukocytes and a dense network of fibrin in which numerous bacteria can be found, and the third layer includes the necrotic epithelial surface, again showing the meshwork of fibrin. It is this fibrinous involvement of the epithelium that makes the pseudomembrane so adherent and leads to denudation of the necrotic epithelium and to exposure of the vascular stroma when the membrane is removed. A striking histologic characteristic is the site of the bacteria which are almost entirely confined to the outer layers of the membrane.

The inflammatory reaction, consisting of severe edema and congestion and varying amounts of exudate, extends irregularly into the dermis and underlying tissue. The reaction is due to the toxins of the bacillus and not to the organism itself.

The histologic picture is the same no matter which portion of the mucosa is involved. A significant point is that in laryngeal diphtheria the pseudomembrane and underlying edema may be obstructive. The infection limited to the nose, while generally milder clinically, is dangerous because it may be overlooked and, in the absence of treatment, may result in serious toxemia. It is possible for the infection to spread from the pharynx through the eustachian tube to the middle ear. Infection of the external auditory canal is rare, but it may be produced by invasion from the middle ear through a ruptured tympanic membrane.

Death during the active phase of the disease is due either to overwhelming toxemia or to suffocation. The great danger in the convalescent period is an irreversible effect of the toxin on the myocardium. Paralysis results from involvement of the peripheral nerves, particularly of the pharynx, manifested clinically by difficulty in swallowing. In young children a serious complication in diphtheria is secondary infection by hemolytic streptococci. This combination of infections produces a fulminant disease that may involve the lungs.

Diphtheria of the skin is relatively common in the tropics and was a serious problem during the war. Material was received at the Armed Forces Institute of Pathology from several individuals who had died of toxemia before the nature of the skin lesion was recognized. Dermal diphtheria is characterized clinically by a thick, tough, densely adherent black membrane. After it is removed the granulating ulcer that remains is very refractory to treatment. Plastic repair is frequently necessary in order to effect a cure.

Tuberculosis of the pharynx is discussed in Chapter 2. The comprehensive review by Szanto and Hollender and Myerson's text on tuberculosis of the ear, nose and throat should also be read.

Syphilis in the second stage involves the pharynx as mucous patches, less commonly as an extension to the nasopharynx as the less specific syphilitic rhinitis. The tertiary manifestations are either gummatous or a diffuse interstitial inflammation. Either of these on healing may cause serious deformity by adhesions and contractions, especially in the nasopharynx.

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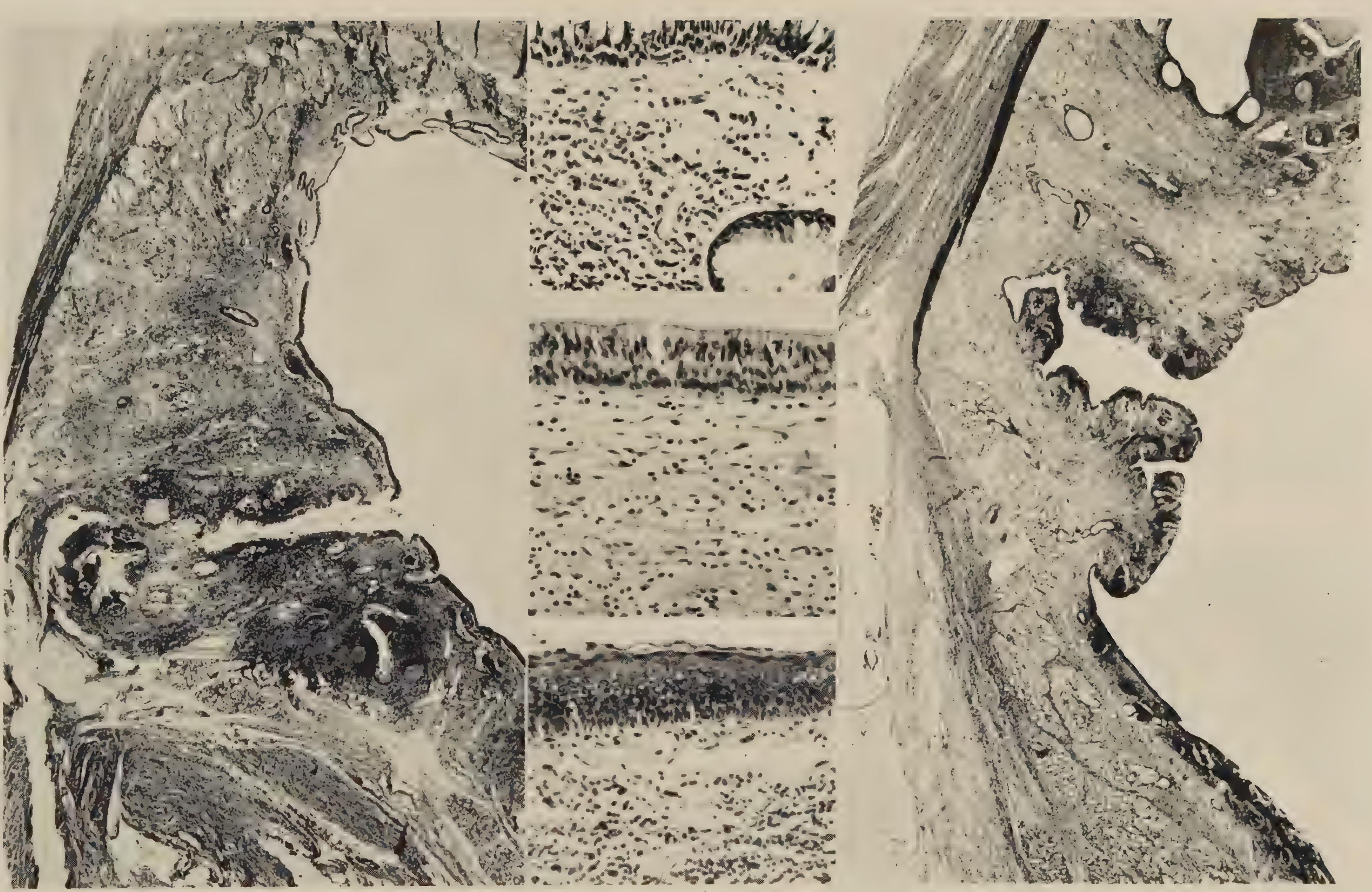
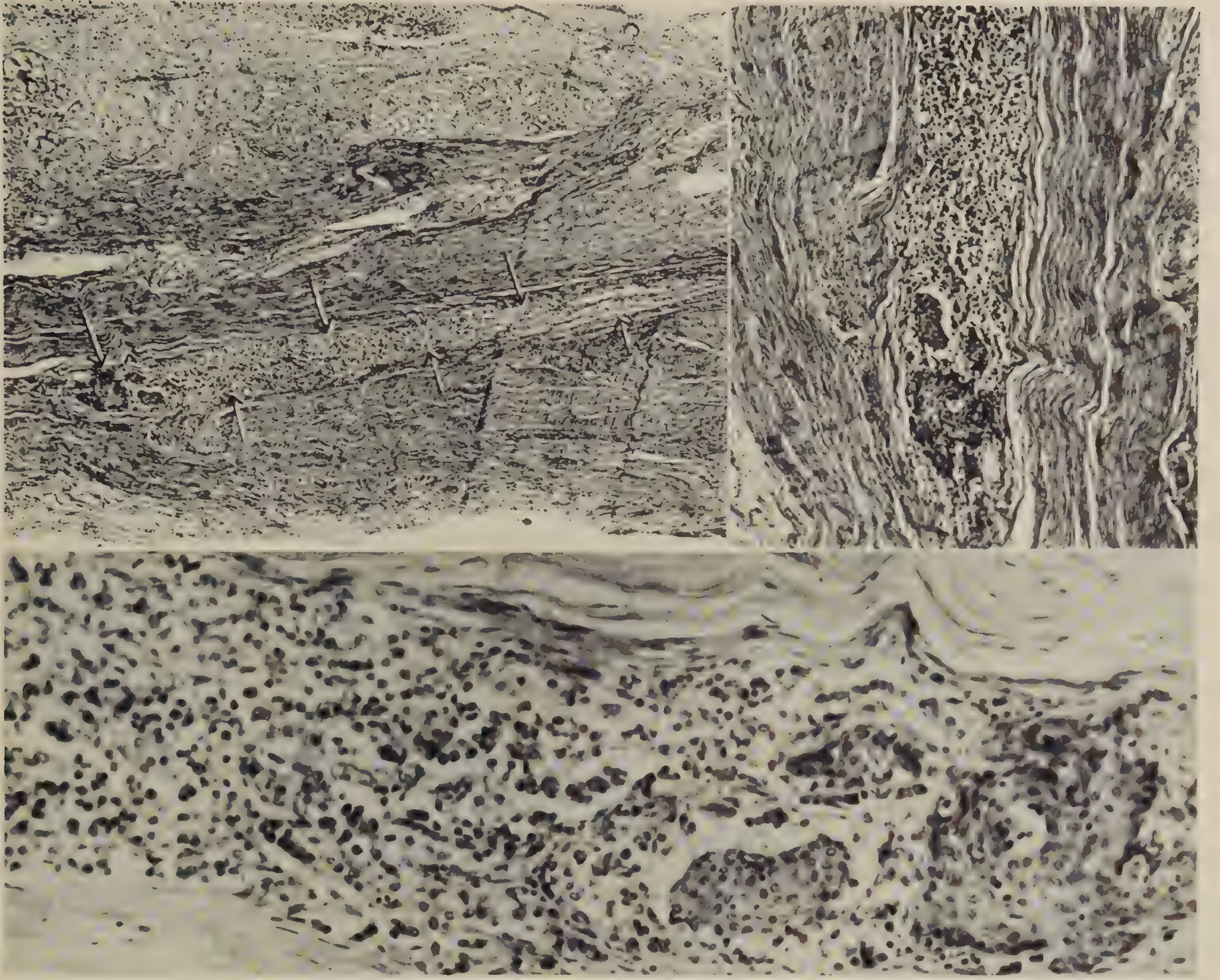


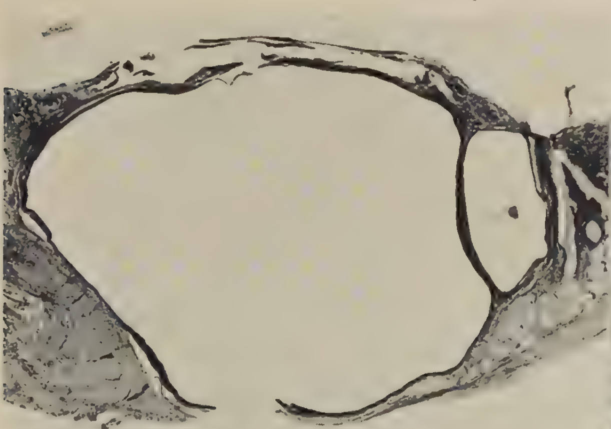
Superior and proximal posterior walls of nasopharynx, longitudinal midline sections of 2 cases with proximal (nasal) parts at top and distal nasopharyngeal segments including prevertebral fascia at bottom. Numerous seromucinous glands lie deep in mucosa. **Left,** the deep crypt-like space which extends almost to the fascia represents a large **median nasopharyngeal recess** rather than a true nasopharyngeal bursa, which is very rare. In this location these structures may be clinically indistinguishable. Walls of the median recess contain abundant diffuse lymphatic tissue including numerous lymph follicles, presumptive evidence of involuting nasopharyngeal tonsilar tissue. x 11. **Right,** the upward and backward direction of the central diverticulum-like process and its location at the inferior margin of the pharyngeal tonsil are compatible with pharyngeal bursa, but it probably is a large median recess. x 13. **Center,** fields which show types of epithelium in the upper, middle and lower portions of the section on the left. *Top,* ciliated respiratory epithelium with numerous goblet cells in parts of the proximal nasopharynx. *Middle,* typical ciliated pseudostratified columnar epithelium, the predominant type. *Bottom,* the stratified squamous epithelium of the distal oropharyngeal segment. All x 145. (Both sections from R. A. Moore, St. Louis.)

PHARYNGEAL PITUITARY

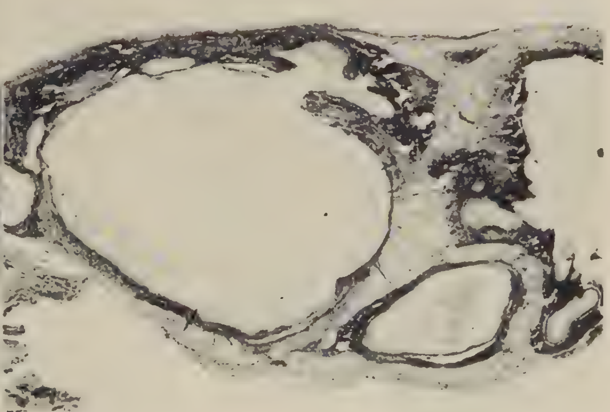
CYSTS, NASOPHARYNX



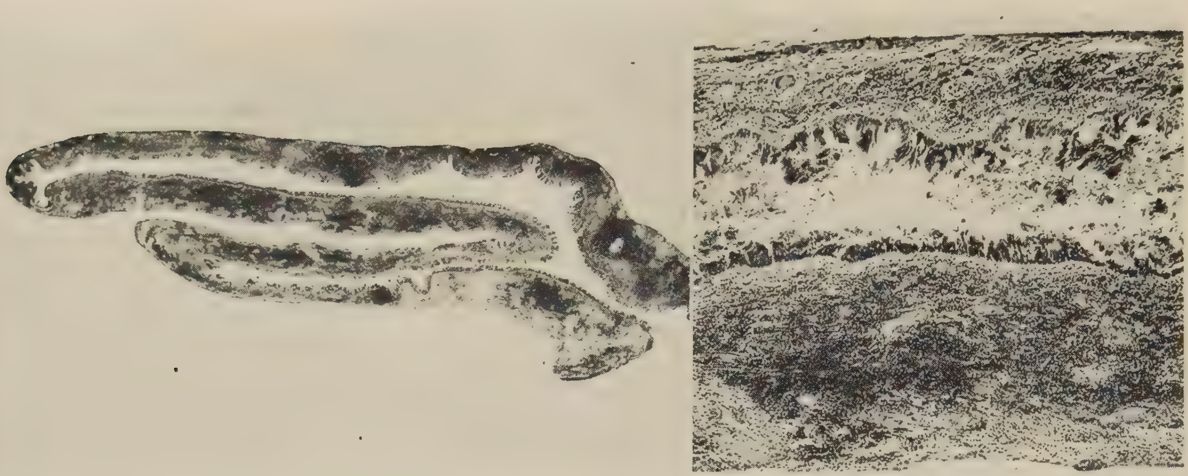
Pharyngeal pituitary. Small masses of typical and atypical pituitary tissue, derived from epithelium of Rathke's pouch, remain in the mucosa of the nasopharynx over the vomerosphenoidal articulation in the midline. *Upper:* most typical location, deep in the mucosa and extending into the periosteum *(arrows).* x34, x55. *Lower:* cells similar to those in anterior pituitary. Nests of undifferentiated epithelium are frequently present, as above; glandular structures less commonly. x55. (R.A. Moore, St. Louis.)



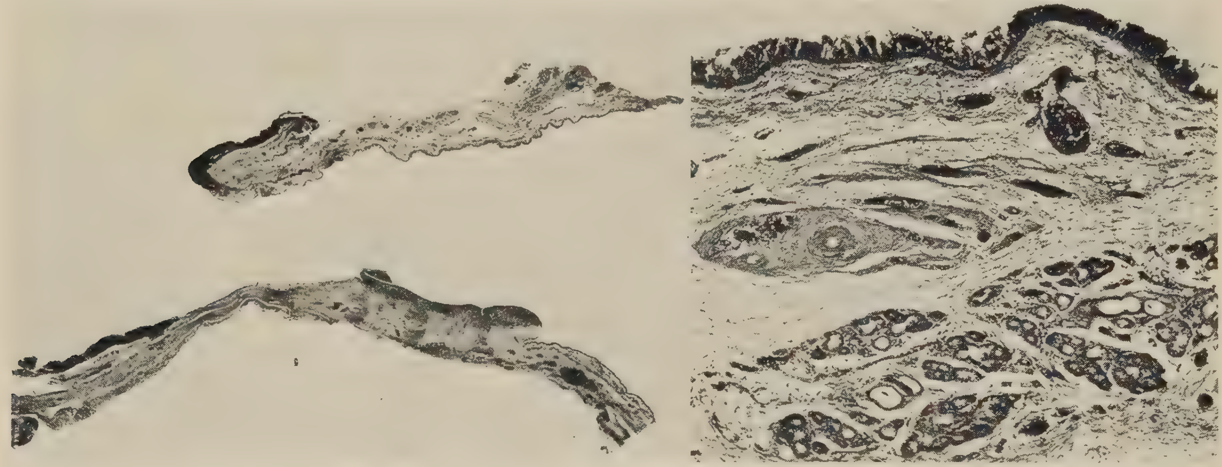
Cyst, posterior pharyngeal wall, extending to periosteum below. Possibly a cystic pharyngeal bursa. Anterior part of specimen at right; surface epithelium at top. x7.



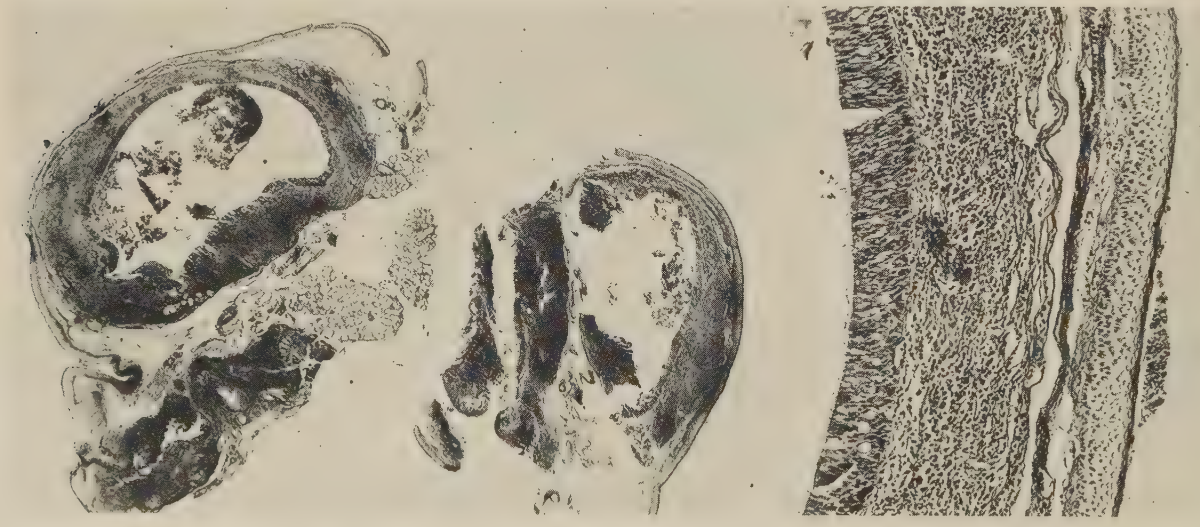
Retention cysts in nasopharynx of patient with extensive carcinoma in fossa of Rosenmüller, pterygomaxilary fossa, eustachian tube, and other parts of temporal bone. x8.



Pharyngeal diverticulum or branchial cleft sinus with patent internal (pharyngeal) orifice. Collapsed sac from a 52 year old white man with carcinoma of the larynx. x 8. The pseudostratified columnar epithelium is intimately related to a layer of diffuse lymphatic tissue, as in branchial cleft cysts and sinuses. x 55.

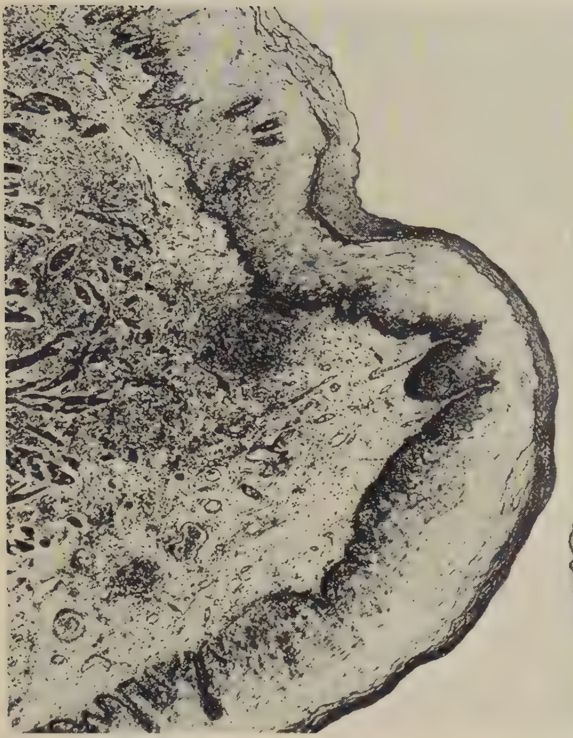


Pharyngeal diverticulum or pharyngocele. Portions of excised sac. Clinically, an intermittent swelling anterior to sternomastoid muscle just beneath angle of mandible in 43 year old man. x 4. Lining of respiratory epithelium with seromucinous glands and ducts of normal structure. x 48.

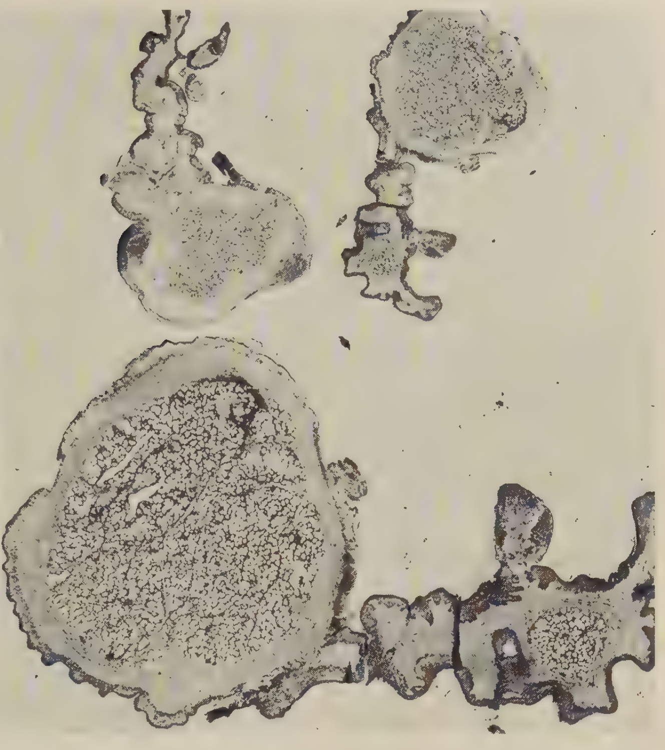


Branchial cleft cyst that presented as a mass in the posterior tonsillar pillar of a 36 year old man. Thick layer of lymphatic tissue surrounds epithelial lining. Note other branchiogenic remnants in lower left field. x 11. Segment of cyst wall with lining of ciliated pseudostratified columnar epithelium at left, in intimate contact with lymphatic tissue layer. Squamous epithelium of pharyngeal surface at right. x 75.

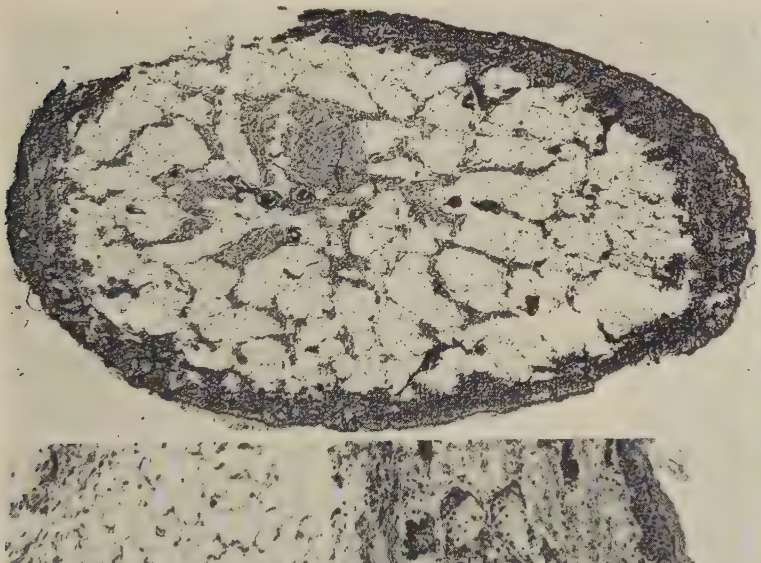
VARIED POLYPOID LESIONS



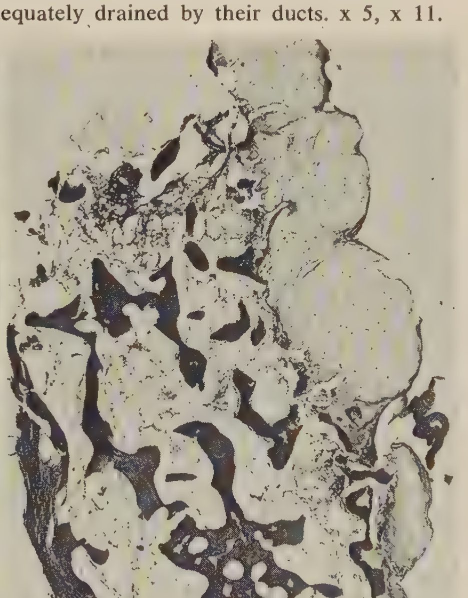
Fibrous polyp, pharynx. Edematous vascular stroma with delicate muscle bundles and collections of inflammatory cells. Thick squamous epithelium covers surface. x 31. (Louis Dailey, Houston, Tex.)



Pedunculated glandular hamartoma, tonsillar region of a 3 year old boy. Dense fibrous tissue about overdeveloped collections of mucous glands with abnormal histologic structure, but apparently adequately drained by their ducts. x 5, x 11.



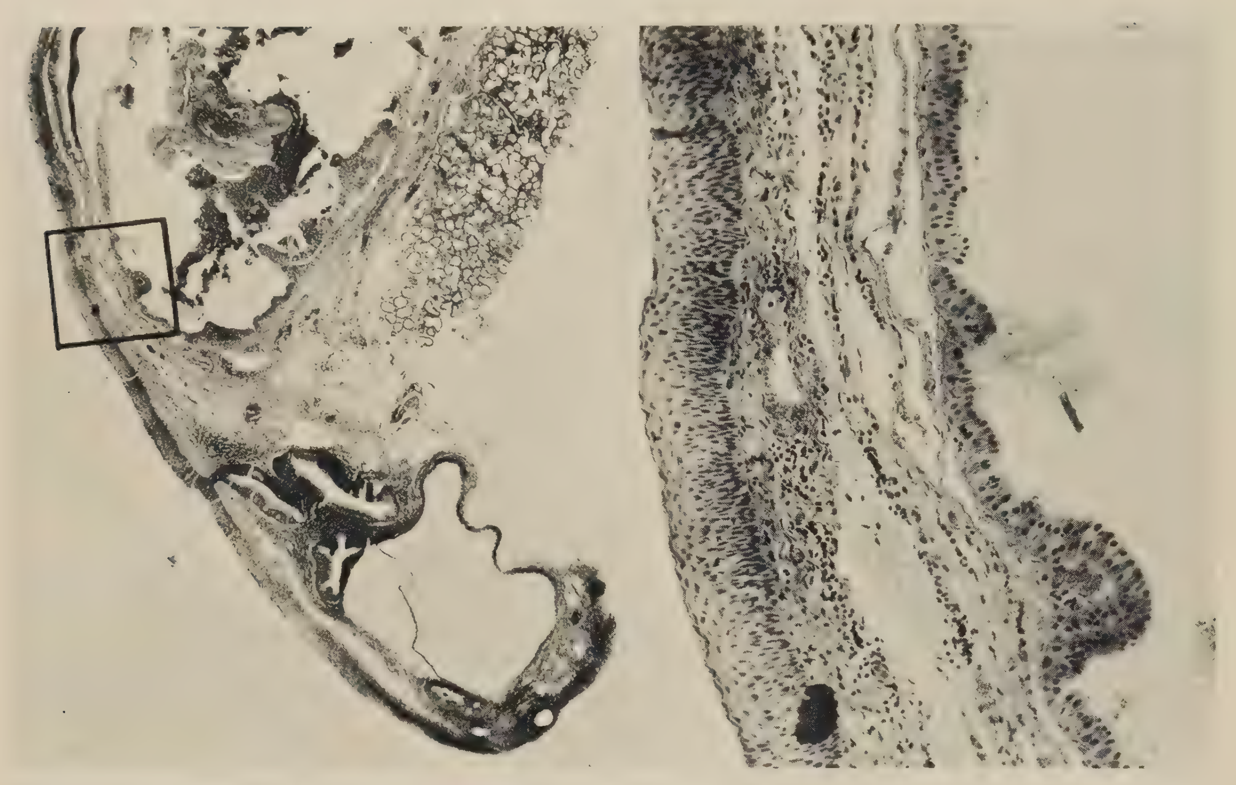
Dermoid, nasopharynx of a 2 day old infant. Pedunculated mass present at birth, in region of eustachian cushion. Central mass of fat tissue with fibrovascular septa, is covered by skin containing well developed hair follicles and sebaceous glands. x 9, x 75. Termed “hairy polyp” if hairs are numerous.



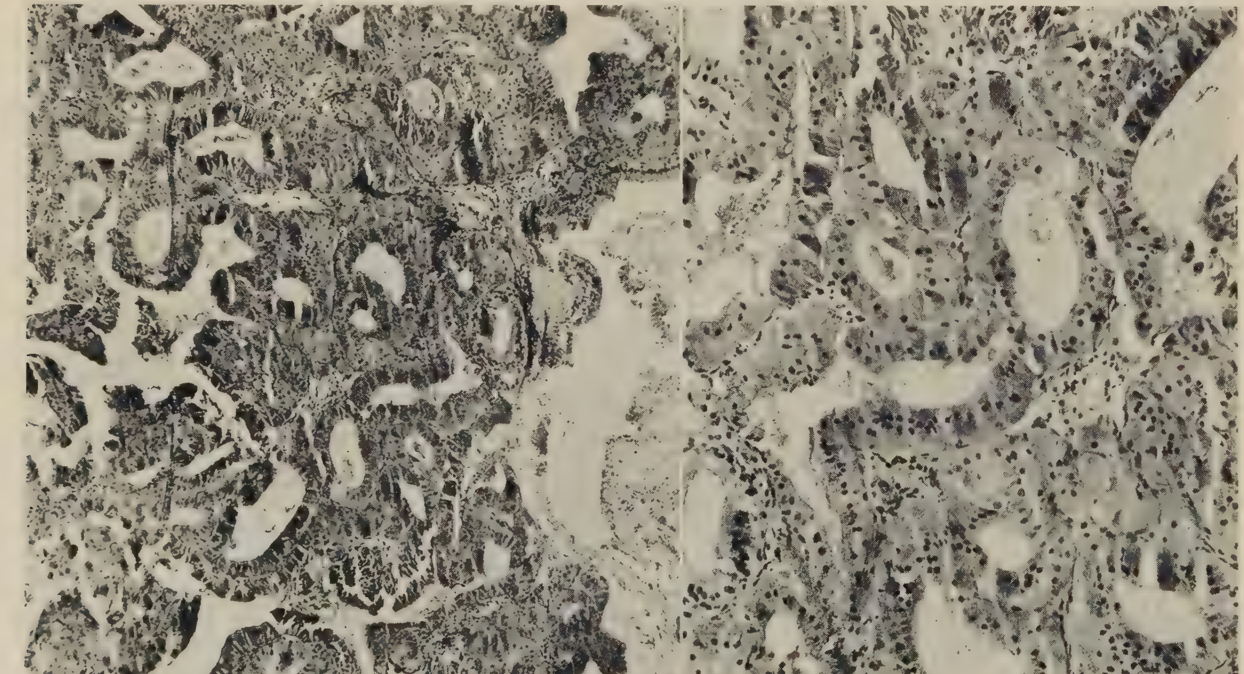
Osteochondroma, presenting as a polypoid tumor in tonsillar fossa of 19 year old male; on x-ray, continuous with anterior part of a cervical vertebra. Well differentiated cartilage cap and cancellous bone. x 24.

PAPILLARY CYSTADENOMA, PHARYNX

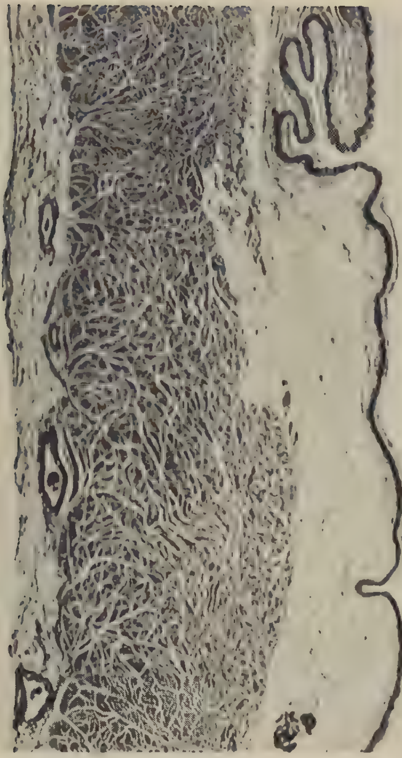
(ONCOCYTOMA: OXYPHIL ADENOMA)



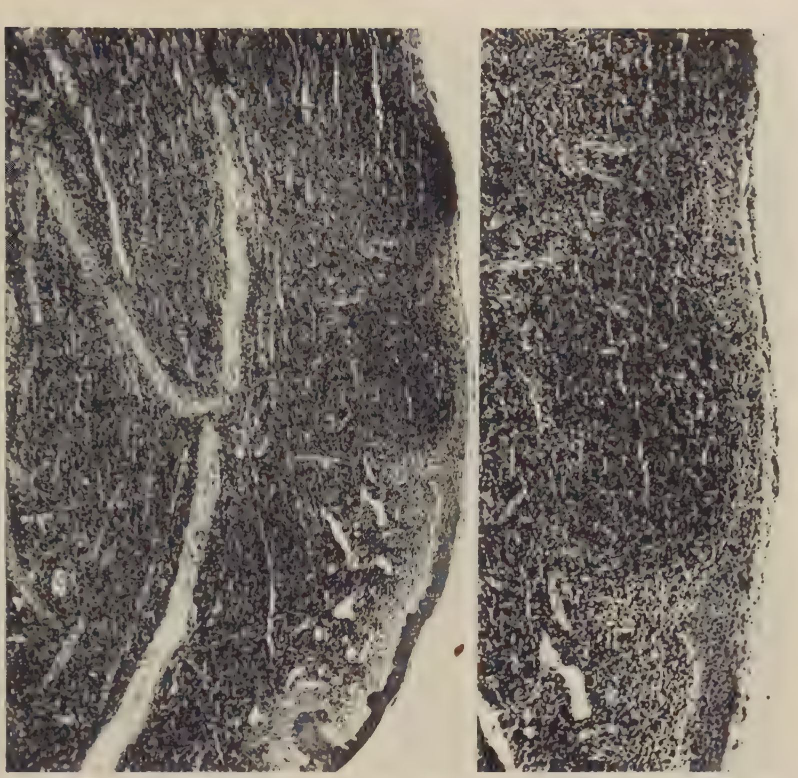
Papillary cystadenoma (top) and branchial cyst and inclusions (bottom). The papillary cystic structure may have arisen from ducts of "minor salivary gland" or may be branchiogenous. x 28. Detail of blocked area: surface squamous epithelium at left, that lining cyst at right. Latter with its double row of uniform nuclei and brightly eosinophilic cytoplasm resembles epithelium of Warthin's tumor and of salivary gland ducts. x 160.



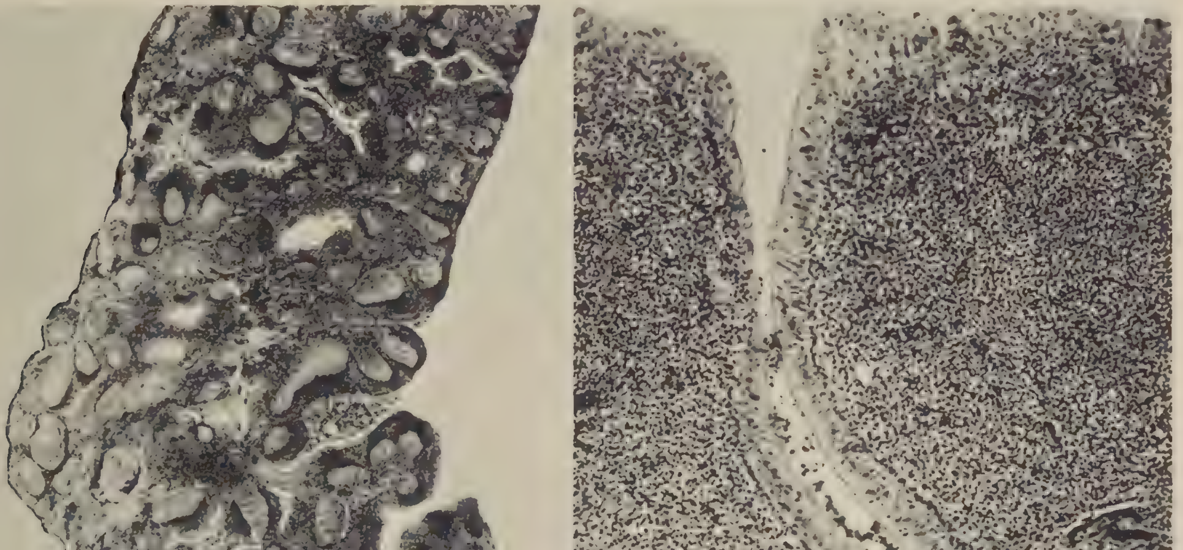
Papillary cystadenoma (oxyphil adenoma; oncoytoma), nasopharynx, probably arising from duct of "minor salivary gland" in 80 year old man. Clinically, a bluish, pebbled, pedunculated mass behind left eustachian cushion. Solid area. x 70. The gland elements resemble the epithelium seen in salivary gland ducts and Warthin's tumor. x 160.



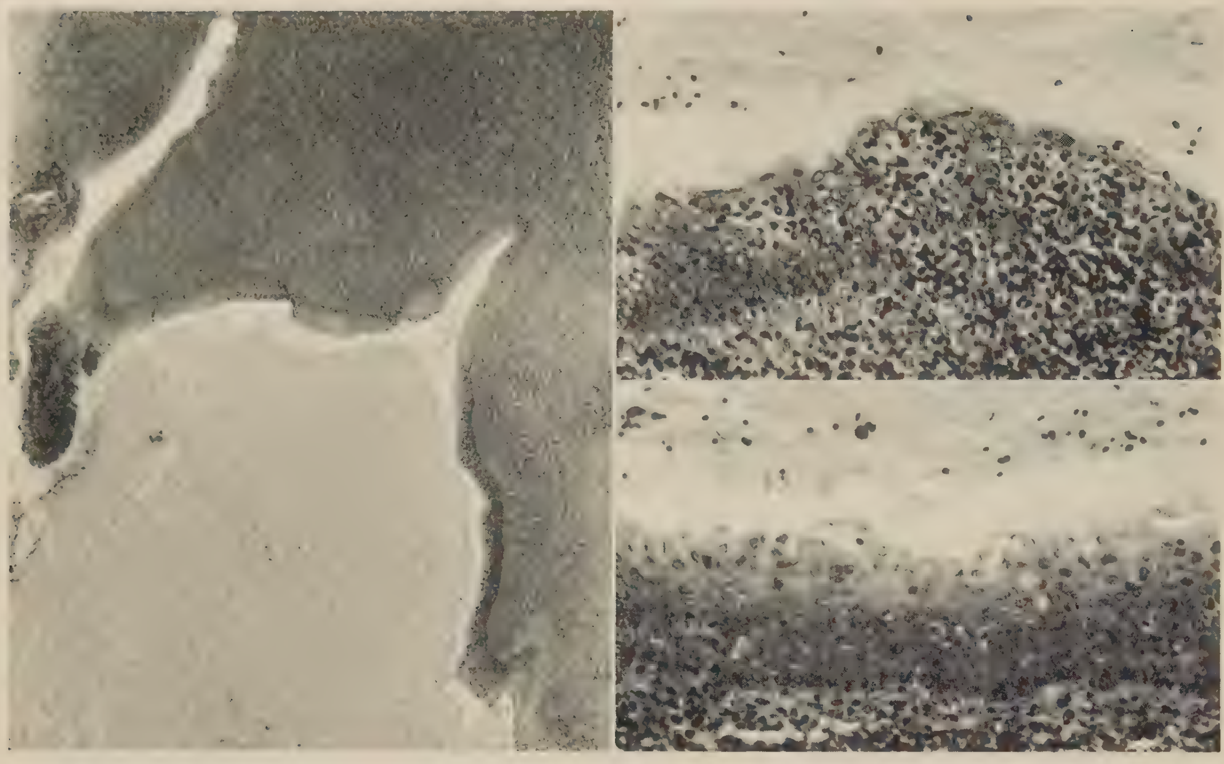
Posterior pharyngeal wall. Squamous epithelium up to the crypts; striated muscle layer; thick prevertebral fascia. x 8.



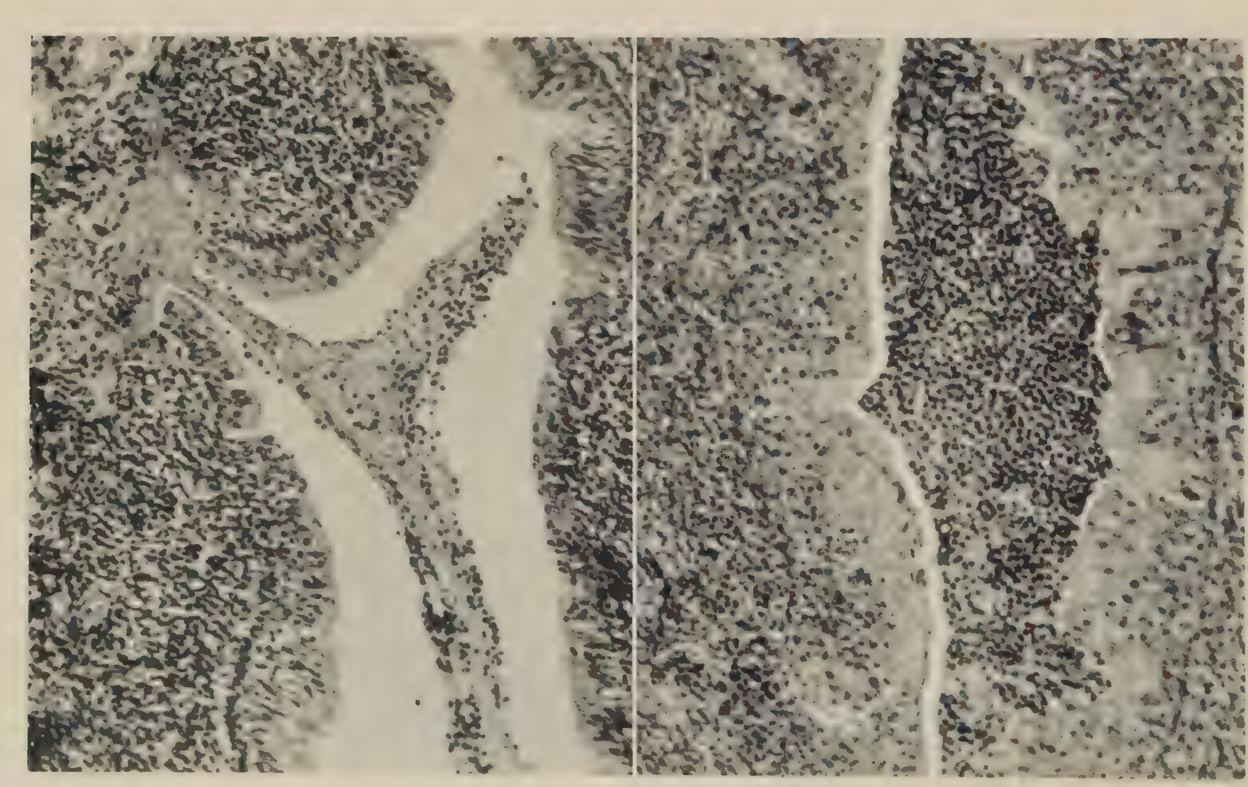
Mucosa of nasopharynx. A. Hyperplasia of lymphatic elements; squamous metaplasia of epithelium. x 48. B. Primary lymphatic follicle causing slight elevation of surface and closely related to overlying epithelium. x 70.



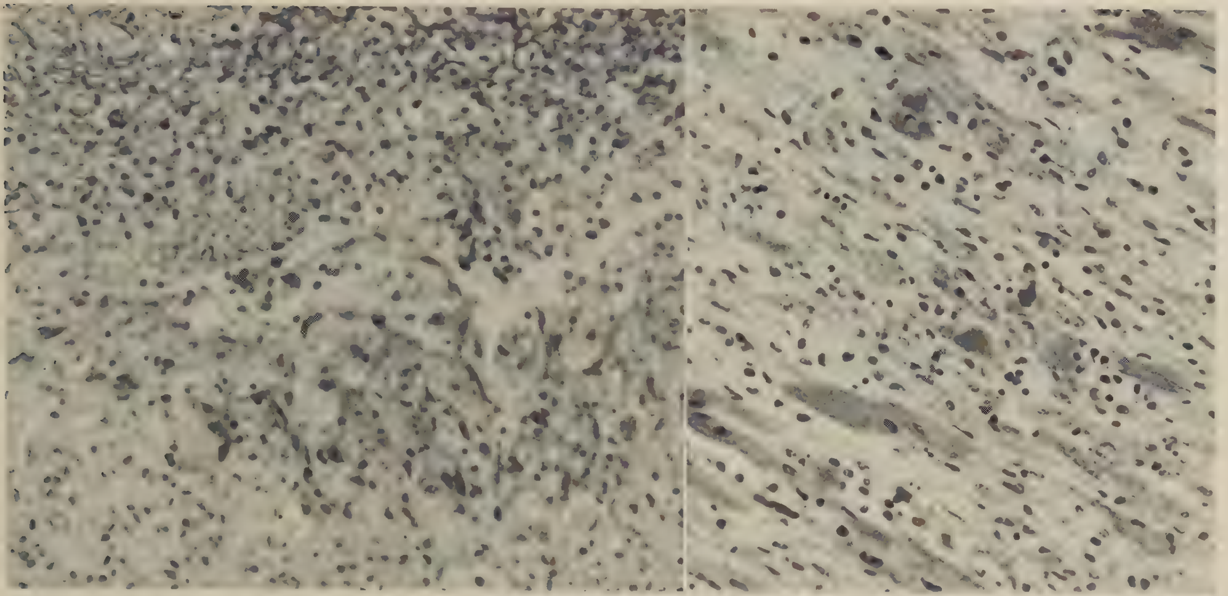
Relatively normal pharyngeal tonsil (adenoid) with diffuse lymphatic tissue containing numerous follicles with germinal centers. Surface epithelium and the folds are lined by ciliated respiratory epithelium with occasional small patches of stratified squamous epithelium. x 10. Note abundant lymphocytic infiltration of epithelium, particularly prominent on the crests of the folds. x 95.



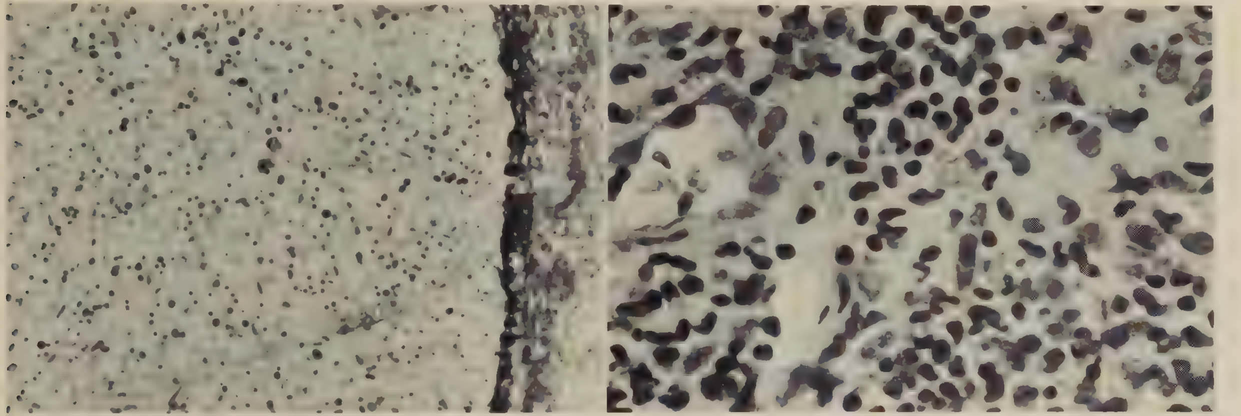
Tornwaldt's disease, with occlusion of bursal orifice. Accumulated secretion, in this case, has formed a retention cyst; if it becomes infected, abscess may develop. x 34. The bursa is lined by modified respiratory epithelium. Lymphocytes are infiltrating the epithelium. x 185.



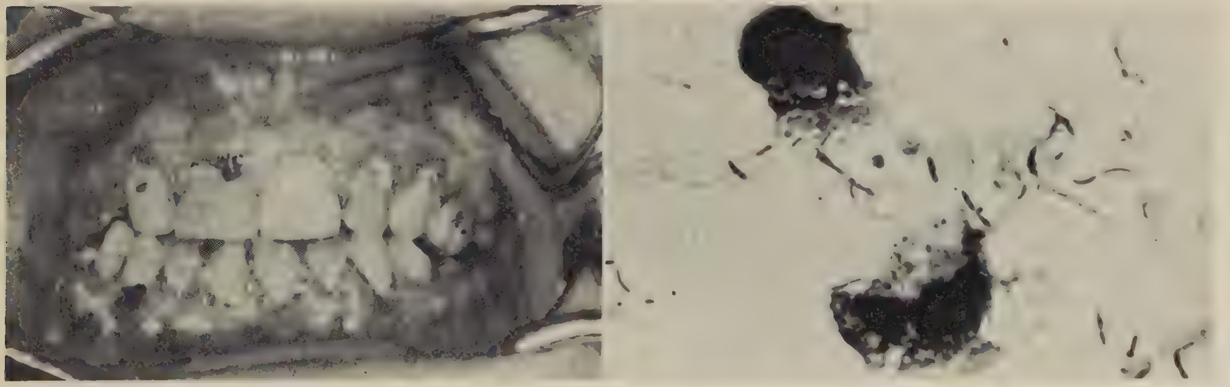
Higher magnifications of the bursal lining. A mild chronic inflammatory reaction has led to accumulation of a little mucus and some lymphocytes in the lumens. x 165, x 185.



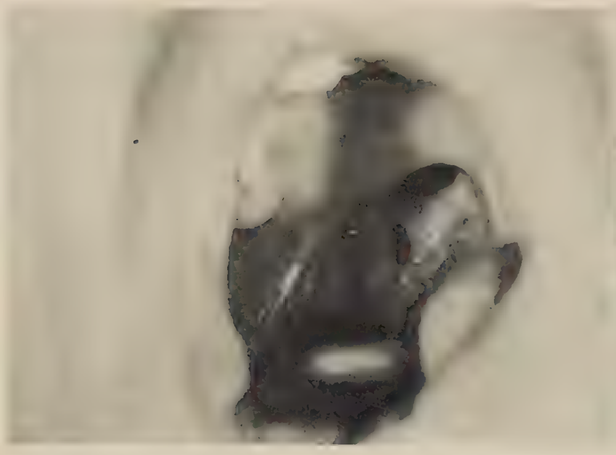
Pharyngeal diphtheria, untreated four days, in 3 year old child. Tonsils and larynx also involved. *Left:* pseudomembrane (at top) fused with few remaining necrotic epithelial cells at left; separated from denuded exposed stroma at right. x280. *Right:* fatal myocarditis due to circulating toxin in upper respiratory infection with *Corynebacterium diphtheriae gravis.* Interstitial edema, cellular infiltrate, necrosis and degeneration of cardiac fibers. x275.



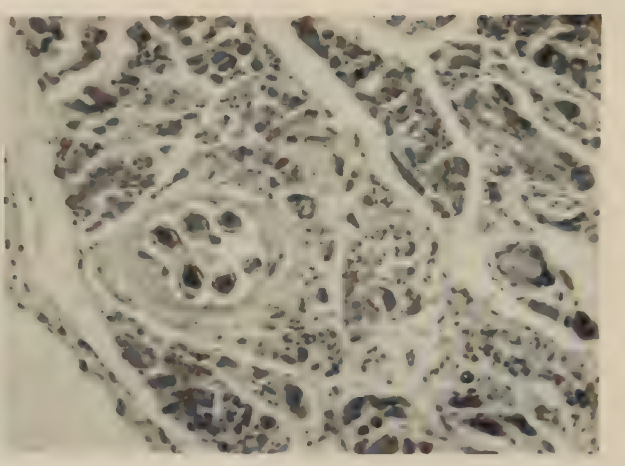
Fulminant agranulocytosis (agranulocytic angina) of undetermined etiology in a 13 year old girl with sore throat, chills, fever; death in one month. Gangrenous ulcerations in upper respiratory tract. Necrotic surface membrane. Lymphocytes and mononuclear cells, but complete absence of granulocytes in partially necrotic, edematous stroma. x280, x500.



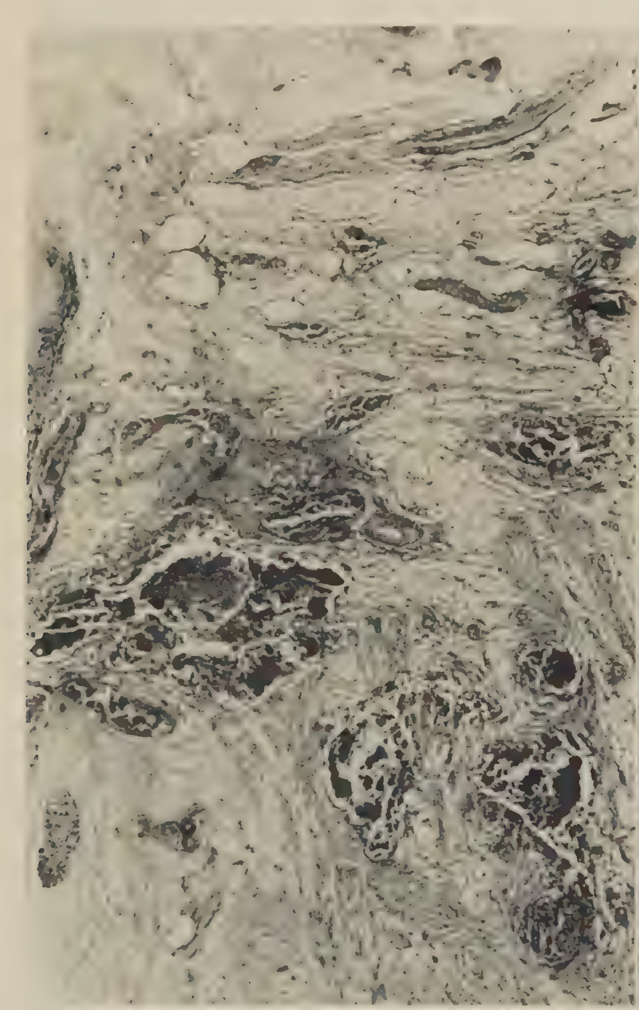
Vincent's infection (trench mouth; fusospirochetosis). Gums swollen and ulcerated, patches of necrotic exudate. Tonsils usually involved; and pharynx, larynx and trachea may be affected. *Right:* organisms of Vincent's infection–spirochetes *(Borrelia vincentii)* acting in symbiosis with fusiform bacilli *(Fusobacterium plauti-vincentii).* x1000.



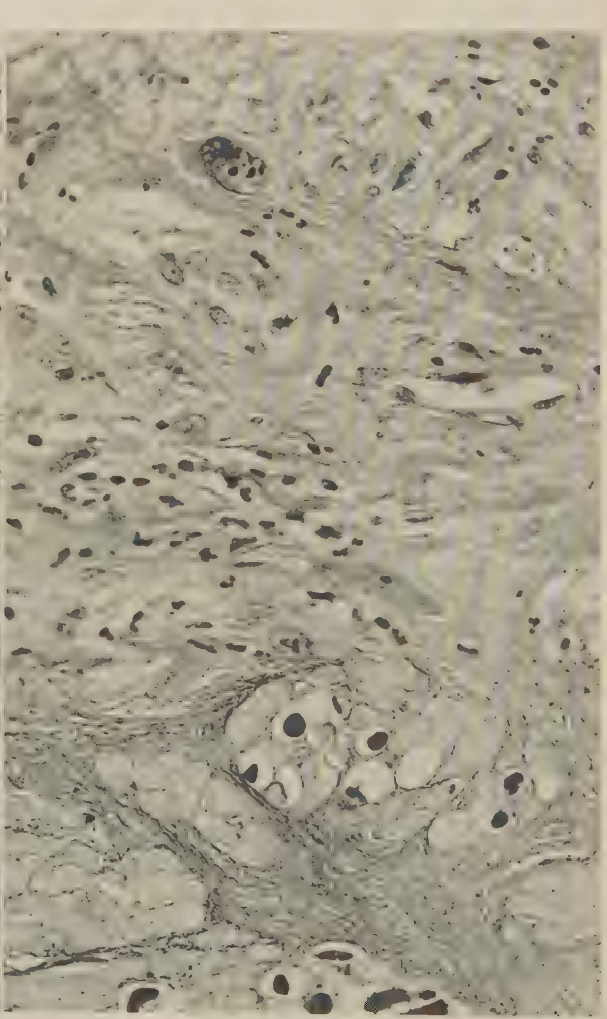
Atresia, pharynx, in congenital syphilis. Dense adhesions bind right side of soft palate to tonsil. Adhesions extend from left pillar to posterior pharyngeal wall.



***Trichinella spiralis* in pharyngeal muscle.** Incidental finding in a 56 year old man who died of carcinoma of the lip. Viable larvae in dense capsule. x 120.



Ludwig's angina. A phlegmonous inflammation, usually a complication following extraction of lower molar teeth. Extension to anterior hypopharyngeal wall. Suppurative thrombophlebitis of all veins and adjacent abscess formation; marked edema and relatively little cellular exudate in other areas of field. x 35. (V. H. Cornell, Washington, D.C.)



Irradiation effect, pharyngeal tissues, of 4500 R and radon implantations 2 and 5 months later. Biopsy 4 months after last treatment: bizarre epithelial cells in basal layer of epithelial mucosa; large stromal cells; swollen vascular endothelium. x 395. Necrotic muscle fibers (black) and interstitial fibrosis. x 75.

CHAPTER 20

TUMORS SPECIFIC TO PHARYNX

Nasopharyngeal fibroma (juvenile or basal fibroid tumor) is one of the few special features of nasopharyngeal pathology. It is a rare tumor, and it is difficult to say at just what age its development begins. Its growth is accelerated at puberty when the clinical symptoms, particularly epistaxis, become more prominent. There is one case in the Registry with onset at the age of six. The tumor occurs predominantly in young males and manifests itself in the prepubertal age and in early adolescence. Some decline to make the diagnosis except in males, but tumors histologically and clinically similar do occur in young females. It is a solitary tumor, usually arising from the nasopharyngeal recess, less frequently from the anterior wall of the sphenoid or from the nasal choanae, or occasionally from any other portion of the nasopharyngeal surface. It must be differentiated clinically from the choanal polyp that arises in the nasal cavity and extends into the nasopharynx.

The tumor is believed to take origin from the fibrocartilaginous tissue of the upper cervical vertebrae or from the fascia basalis located in the pharynx at the base of the skull. This origin has been used to explain the tendency to spontaneous regression at an age when the development of the skull is completed (25 years of age), the theory being that at this time the blood supply of the tumor becomes restricted. This origin has also been used as an explanation of its occurrence predominantly in males, based on the differences in the development of the bones of the face and skull in the sexes.

Nasopharyngeal fibroma is never malignant, but it is a potentially dangerous tumor. In the early stage it grows rapidly and can produce extensive destruction by pressure atrophy. It can invade the skull by this means as well as directly through the basal foramina. It has the capacity for massive hemorrhage, and because of this and its possible widespread distribution its removal can be a major problem. Unless the tumor is small and readily available surgically, the concensus seems to be that it should be treated by hormones or irradiation to bridge over the time until the normal regressive changes make its removal less of a surgical risk.

The evidence gathered from the study of material in the Registry gives a convincing impression that this tumor is primarily vascular rather than fibrous. This would account for the aggressive growth of the tumor and for its propensity to bleed. In the course of time, and particularly during adolescence, the connective tissue element begins to predominate and the blood vessels become less and less conspicuous until eventually the tumor becomes a much reduced, firm fibroma with only the larger and more organized blood vessels remaining. This is the spontaneous regression that is a clinical characteristic. It is claimed by some that regression can be accelerated in the male by the administration of gonadotrophic hormones, but this hormonal relationship and the spontaneous regression are not generally accepted as proven facts.

Grossly, the tumor is sessile, reddish in color from its vascularity, and lobulated. Its consistency depends on the degree of fibrosis, and if this is advanced, it can be cartilaginous. In the earlier stages it is a more delicate structure and bleeds freely.

Microscopically, in the active phases the vascularity is the prominent feature. This begins as large, fully developed vessels at the base that become smaller and less organized until at the surface there is a spongy structure of fragile endothelial channels with few supporting elements. The stroma in this stage is usually edematous and made up of immature fibroblasts including stellate cells. Toward the base there is an increasing amount of collagen. There may be areas of myxoid character in the body of the tumor. In older tumors the vascular elements become less conspicuous, the stroma relatively acellular and made up of collagenous bundles.

The covering epithelium is of the respiratory type of the nasopharynx or may have undergone varying degrees of metaplasia to the squamous. In the earlier tumors ulceration of the surface is frequent, and if it is present the stroma will show a more cellular inflammatory reaction.

Chordoma has its origin from the vestigial remains of the notochord. It can develop, therefore, anywhere along the spinal column from the sacrum to the base of the skull and can project into the cranial cavity from the clivus. The commonest site is in the pelvis and the next commonest is on the posterior pharyngeal wall where it usually has its origin at the junction of the sphenoidal and occipital bones. It is usually attached to the posterior bony pharyngeal wall by a broad base, but it may be pedunculated. It may fill the nasopharynx and extend into the nasal cavity, and it can erode by pressure through the base of the skull and produce neurologic symptoms by compromising the cranial nerves. The tumor has been reported from other portions of the pharynx and mouth, but in these "ectopic" positions it is difficult to identify because it may so closely resemble chondroma. The tumor was originally thought to be of cartilaginous origin. It is slow-growing and usually does not metastasize, but a few cases with widespread dissemination by the blood stream have been reported.

Histologically, it is made up of a variety of cells, the most characteristic of which is large and vacuolated and resembles cells of the notochord or, to some degree, of cartilage. The largest of these contain huge vacuoles and their nuclei are usually small and condensed. These are called physaliforous or chalice cells. There may be so much intracellular mucin that the cell outlines are lost. The variation in the size of the vacuoles gives a bizarre microscopic appearance to the tumor. Some of the cells are columnar and the vacuoles make them resemble goblet epithelium of the intestinal mucosa. This might cause confusion by suggesting an incorrect diagnosis of adenocarcinoma. The secretion of the cells is not true mucin, however, but chondromucin, the intercellular substance of cartilage. The tumor can contain so much intercellular material that it is myxoid and friable. The non-vacuolated cells are polygonal and tend to be cohesive like epithelial cells. The tumor is usually poorly vascularized, has a very irregular connective tissue stroma, may contain areas of hemorrhage and calcification, and is rich in glycogen.

Pharyngeal chordoma is resistant to irradiation and may be difficult to eradicate because of its broad attachment and its tendency to erode the surrounding hard structures. For this reason the prognosis is poor. Recurrence, however, is usually not evident for years, and because of the slow growth of the tumor, death may be long delayed, even after recurrence.

Imperatori has recently reviewed the subject of cervical chordomas and the student should consult his article for further details.

Craniopharyngioma.—Mention has already been made of the pharyngeal pituitary in the roof of the pharynx along the site of Rathke's pouch. This structure is present in ninety-five per cent of individuals, according to Melchionna and Moore. Normally the remains of the epithelial pouch (craniopharyngeal canal) are also present as small masses of epithelium between the two lobes of the pituitary and in its stalk, most commonly in the anterior and superior portions of the anterior lobe. From these, cysts and solid tumors develop. When arising from rests in the stalk of the pituitary, the tumors are suprasellar, the most common location, and when from rests in the anterior lobe, they are intrasellar. Rarely, rests within the body of the sphenoid may give rise to a tumor in that site. The cystic tumors are lined by squamous epithelium of epidermal type which through active keratinization produces the intracranial cholesteatoma. The intrasellar tumors destroy the pituitary and eventually the sella by pressure, and by further growth seriously compromise the surrounding brain structures. Those arising in the infundibulum of the pituitary expand within the circle of Willis and may invade the brain ventricles. The occasional malignant tumor will actively invade the brain tissue and skull and metastasize to more remote parts of the brain and to the cervical lymph nodes. It is more often a tumor of children and young adults.

The solid tumors are either of epidermal epithelium or ameloblastic. There is no agreement, however, that the tumors that resemble ameloblastoma are in reality derived from odontogenic epithelium. The situation is somewhat comparable to the interpretation of certain of the carcinomas of the maxillary sinus. Bone not infrequently develops in the tumors as the result of metaplasia of the stroma.

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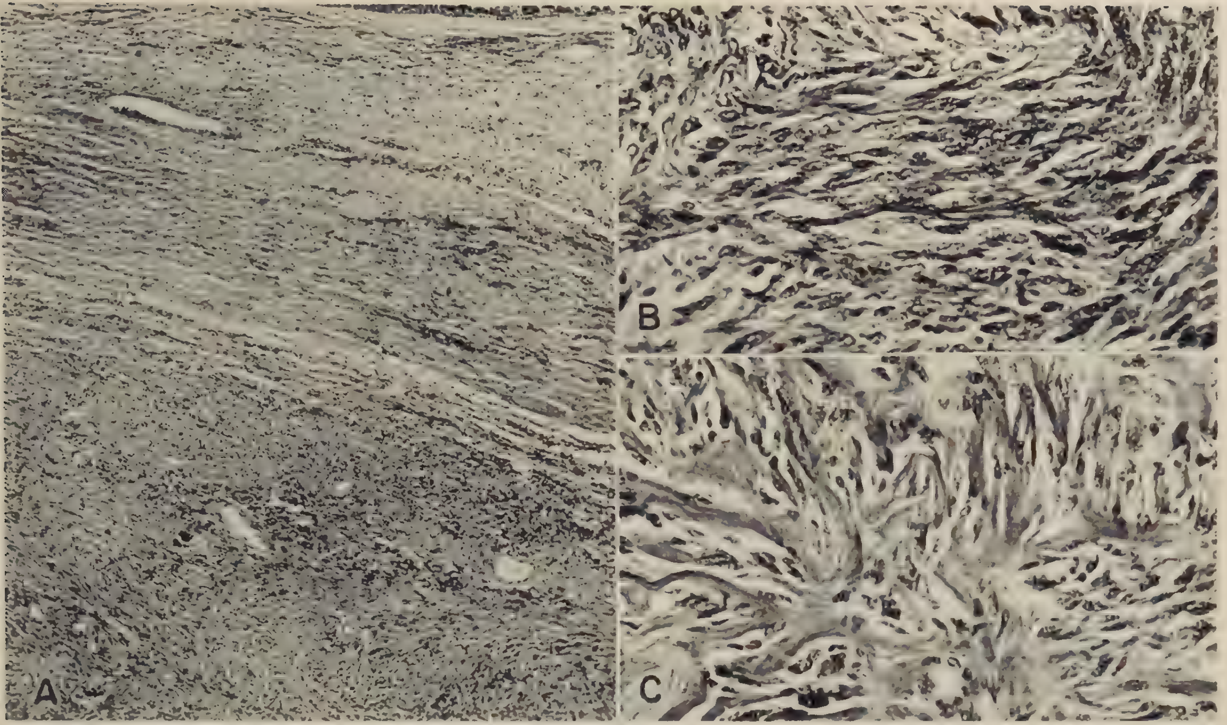
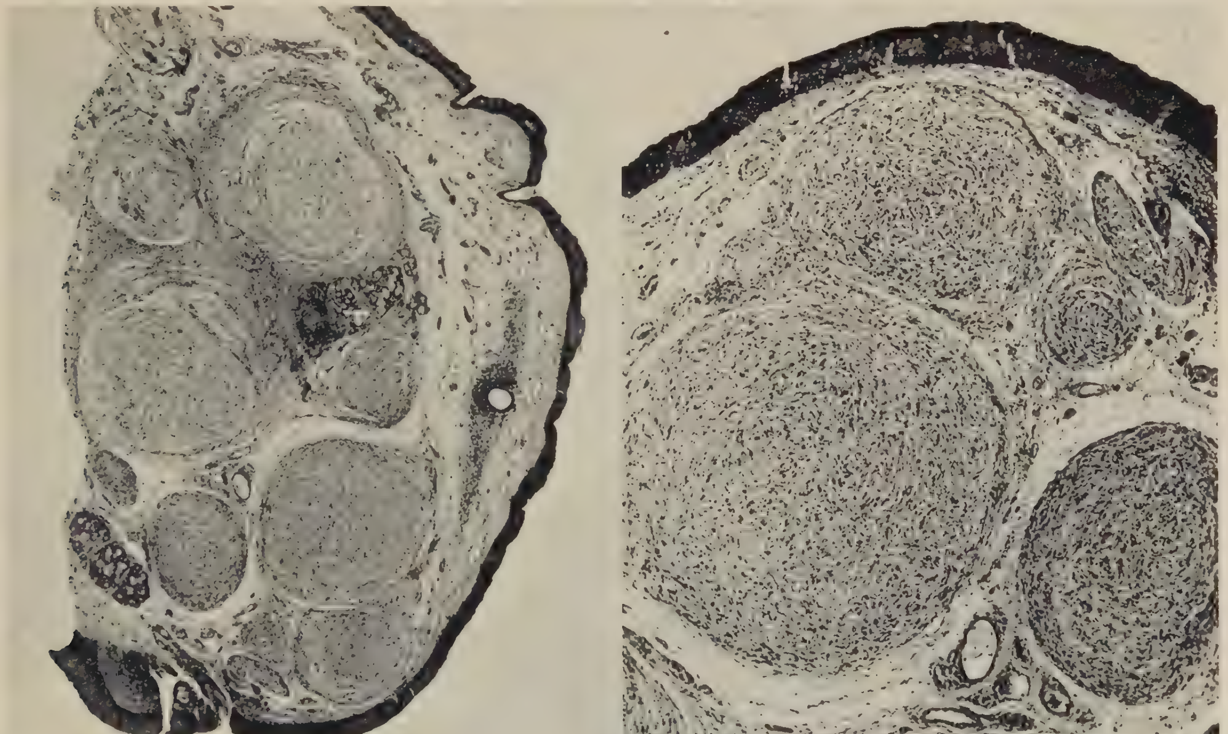
Melchionna, R. H., and Moore, R. A.: The Pharyngeal Pituitary Gland. Am. J. Path., *14:*763–772, 1938.

Schall, L. A., Moderator, Panel Discussion: Nasopharyngeal Fibromata, Clinical Congress, Am. College of Surgeons, New York, September 23, 1952.



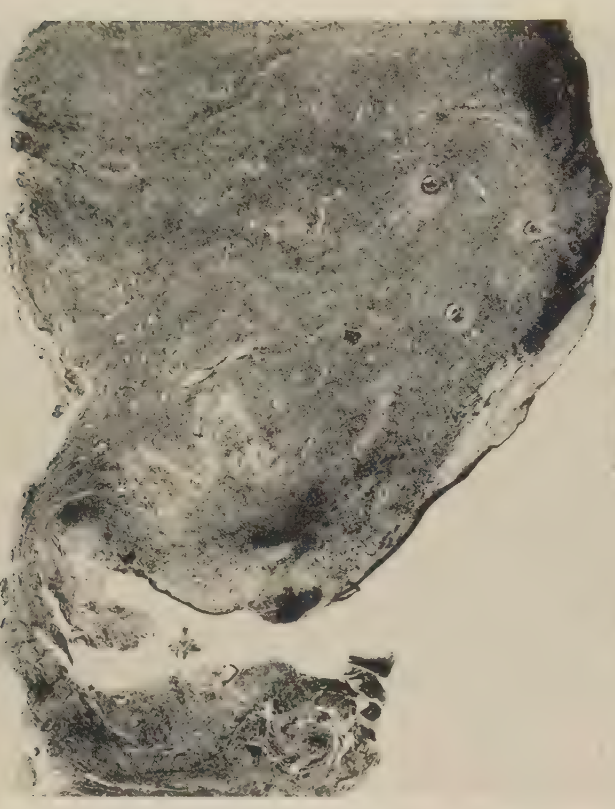
Cellular ("adult") fibroma, nasopharynx, in a 50 year old man. The natural history and histologic features easily differentiate this tumor from juvenile nasopharyngeal angiofibromas. **A.** Cellular tumor with distinct fibrous capsule which blends with overlying mucosa. x48. **B.** Compactly arranged fibroblasts with fibrous processes. x275. **C.** Prominent, partly hyalinized collagen bundles in other areas. No mitoses. x275.



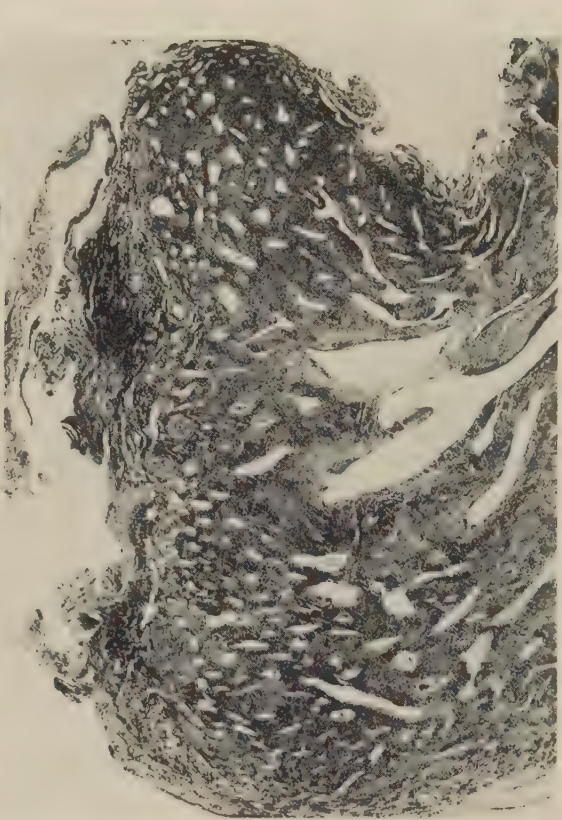
Neurofibroma, oropharynx, in man with numerous subcutaneous tumors over the body **(von Recklinghausen's disease).** Firm sessile tumor of plexiform neurofibroma type. x23. Fibers arranged in small interlacing fascicles. The proliferation of sheath cells and nerve fibers largely within nerve sheaths produces plexiform neurofibroma pattern. x48. (O.B. Hunter, Jr., Washington, D.C.)

JUVENILE NASOPHARYNGEAL ANGIOFIBROMA

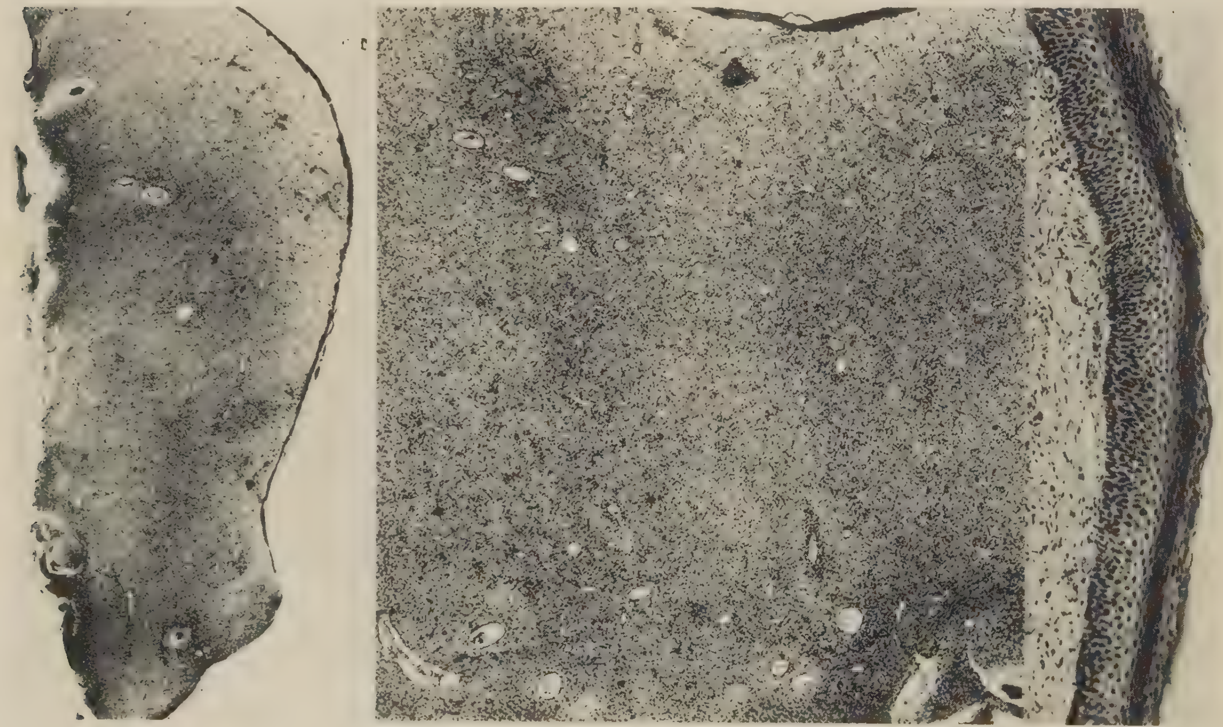
(JUVENILE FIBROMA)



Tumor of fibrotic type from base of sphenoid of a 9 year old boy.

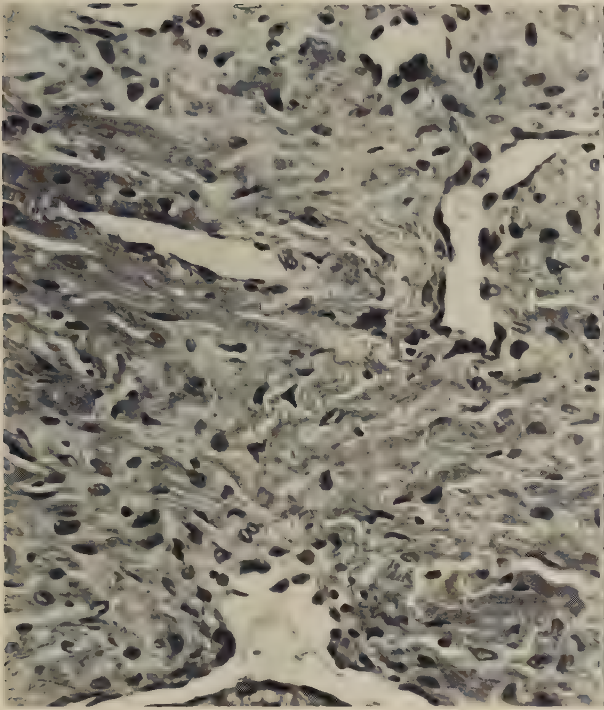


Very large vessels in base of this unusually vascular tumor indicate the danger of surgical procedures. x 17. (W. Putschar, Huntington, W. Va.)

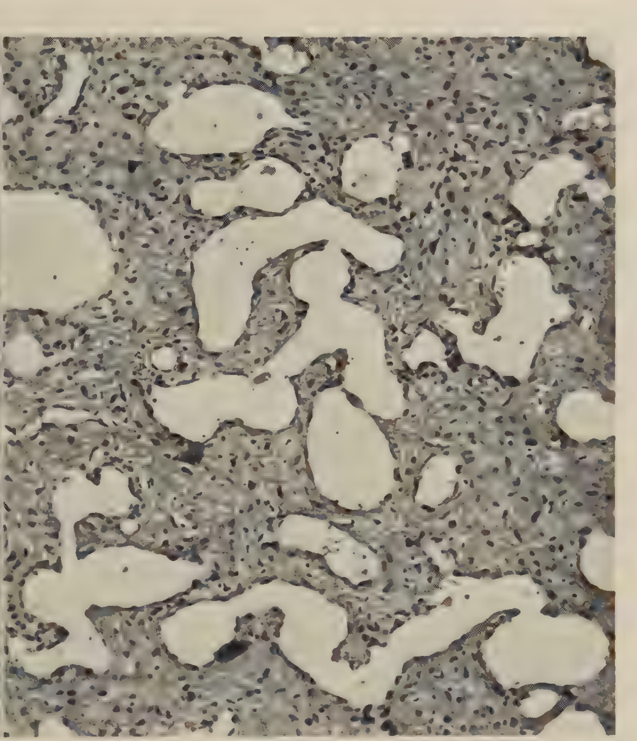


A and B. A more sessile tumor in which the vascular element is less prominent and the stroma very cellular. x 11, x 34. C. Squamous metaplasia of surface epithelium, as seen in another tumor, is a common feature. x 75.

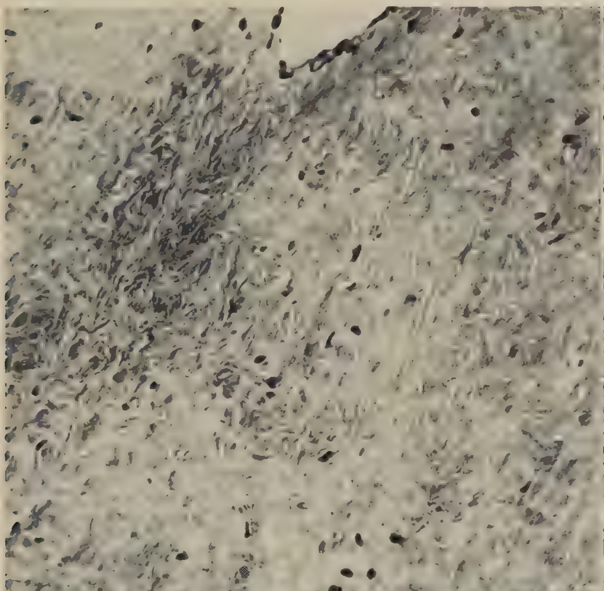
JUVENILE NASOPHARYNGEAL ANGIOFIBROMA
(JUVENILE FIBROMA)



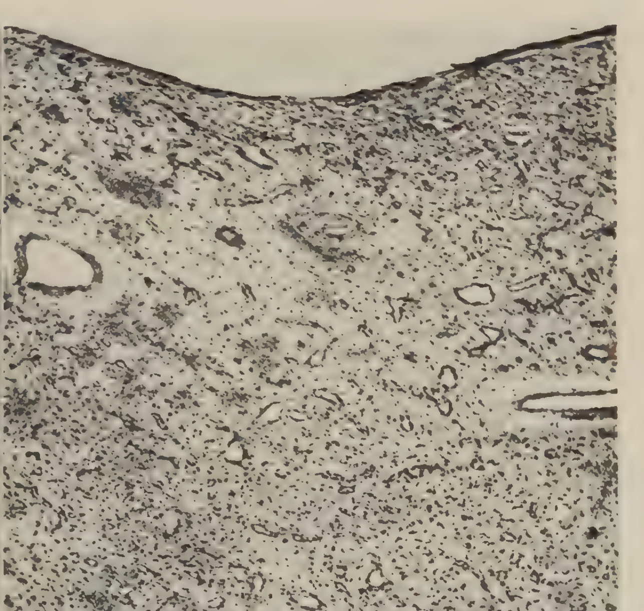
Typical histologic pattern of moderately cellular tumor. Stellate, oval and spindle-shaped cells and wavy, interlacing collagen bundles in intimate contact with branching open vascular spaces lined by a single layer of prominent, often rounded endothelial cells. x 240.



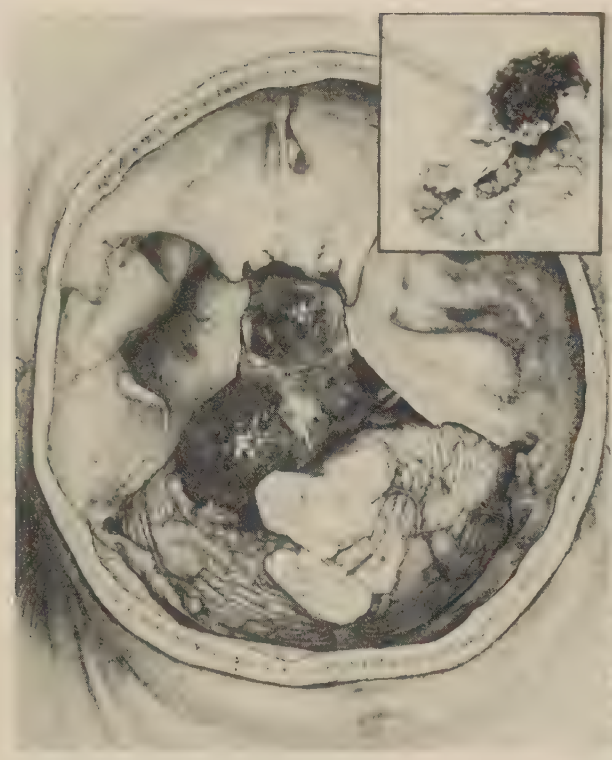
Exaggerated angiomatous pattern present in all parts of the specimen of another case. Fibrocellular component directly opposed to lining endothelium. x 125.



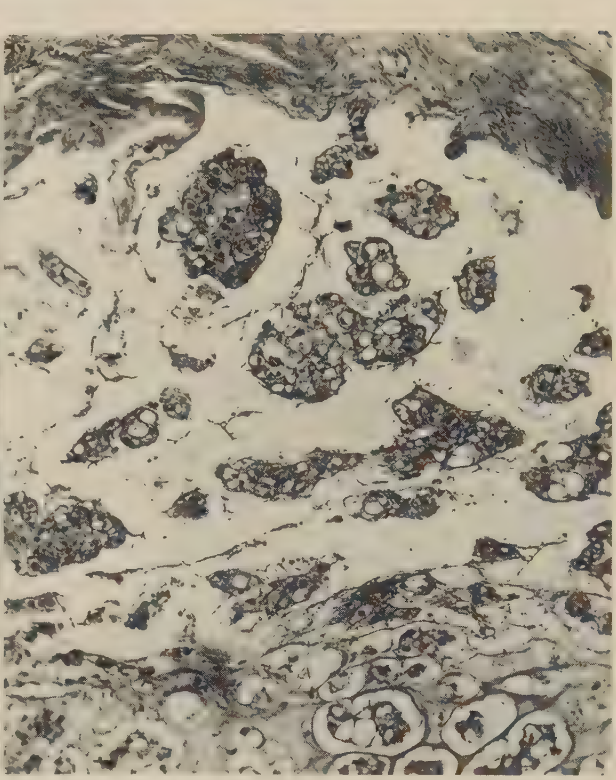
Rare, almost acellular tumor which retains characteristic irregularly intertwining pattern of collagen bundles. x 145.



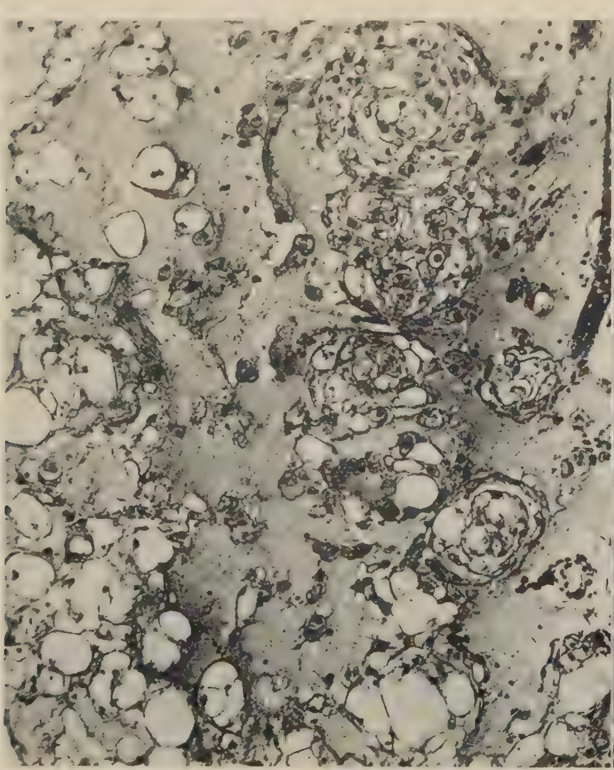
Extension to adjacent structures, particularly the nasal cavity and paranasal sinuses is common and complicates therapy. Tumor (at bottom) blends almost imperceptibly with subepithelial granulation tissue of nasal mucosa, but their microscopic distinction is usually not difficult. x 60.



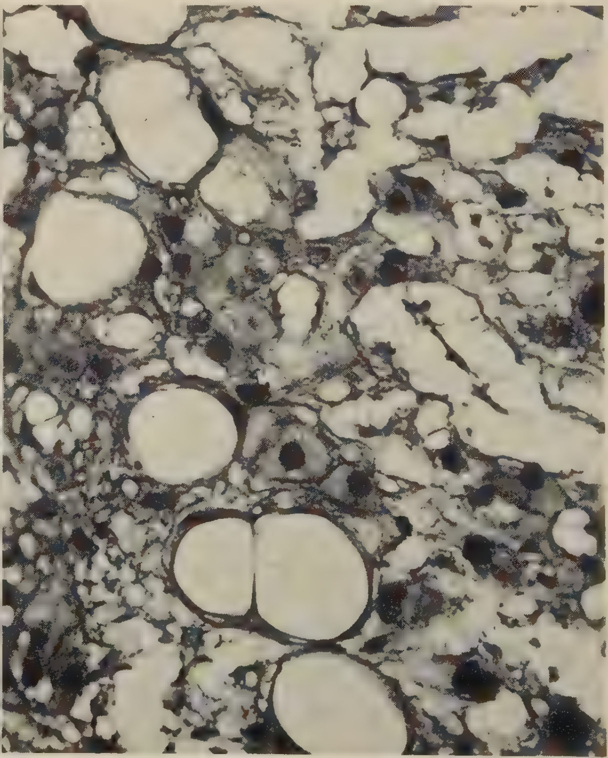
Retropharyngeal chordoma that had eroded intracranially, pushing pons and cerebellum to the right. The inset shows the tumor with the cerebellum and spinal cord.



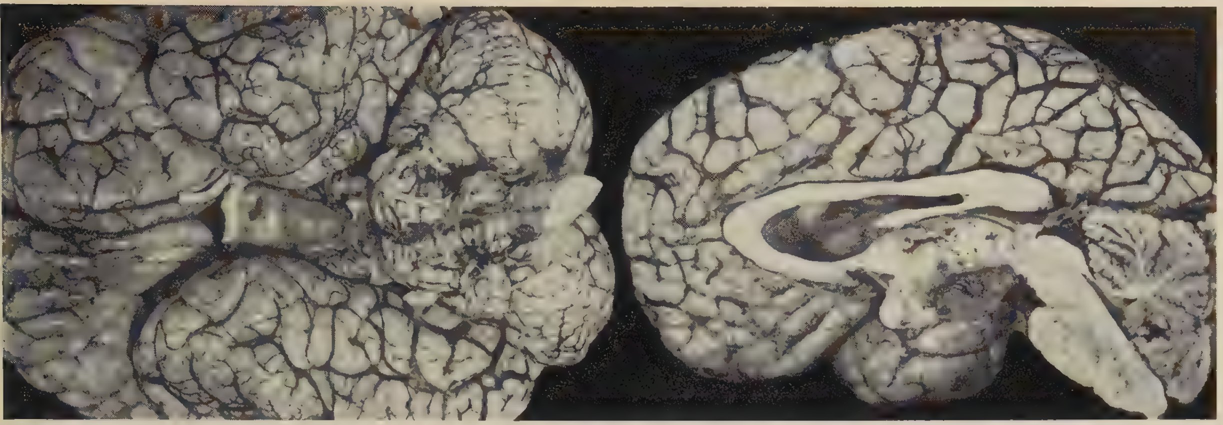
Typical architecture of the chordoma with groups of cartilage-like cells, some containing mucin, in a stroma that varies from free mucin to dense fibrous tissue. x 90.



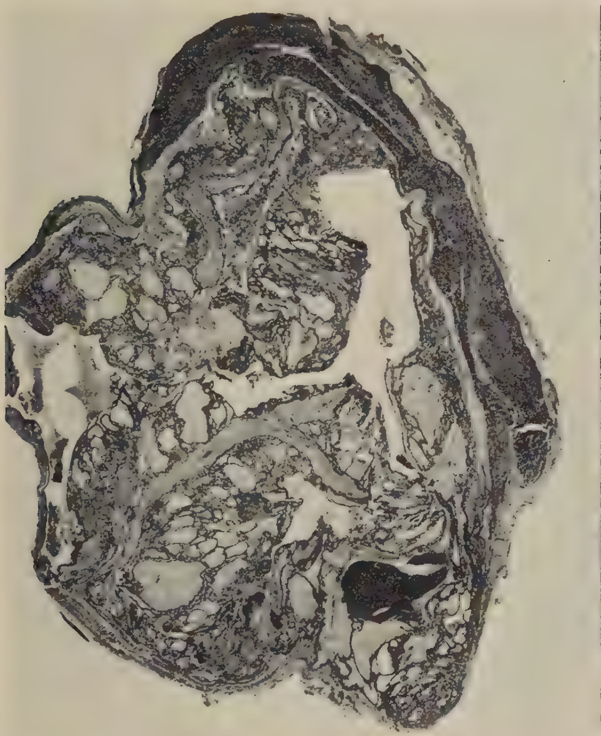
Definitely chondroid stroma and groups of pleomorphic cells, some large and vacuolated. x 150.



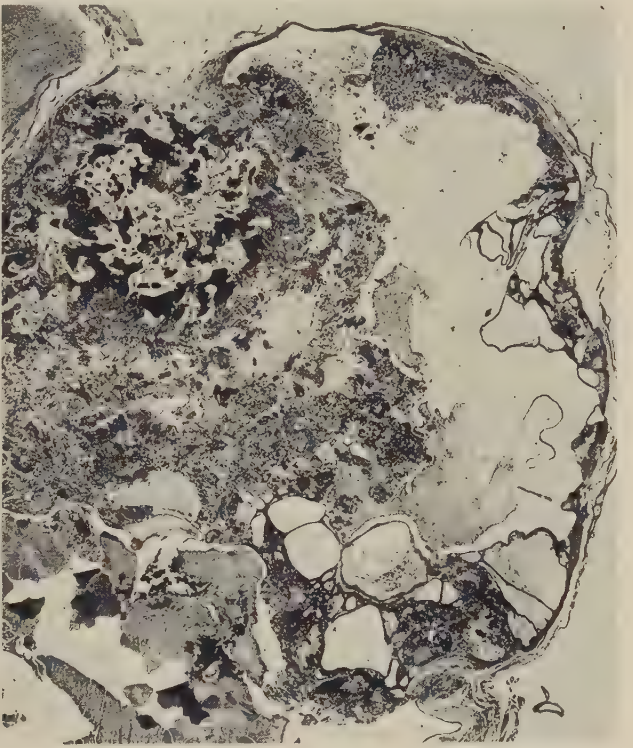
The large vacuolated cells are the chalice cells, a characteristic feature in chordoma. x 400.



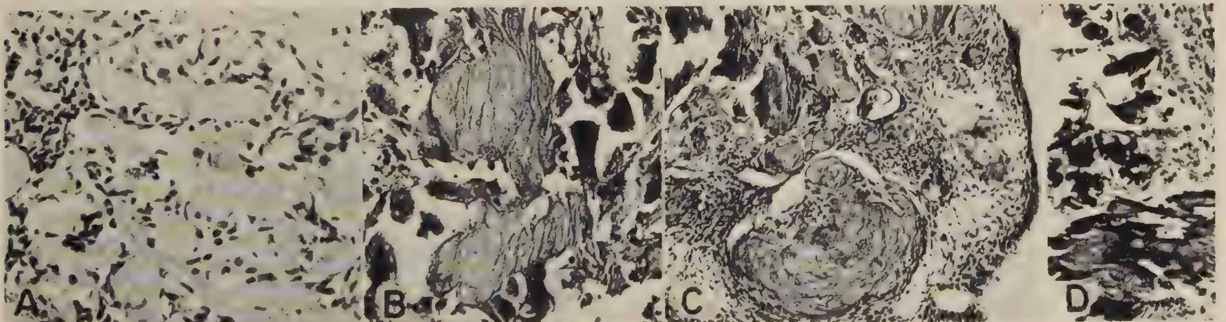
Craniopharyngioma. Tumor at base of brain with anterior displacement of optic chiasm *(left)*. On section, multiloculated cystic mass, compressing and distorting third ventricle: partially gelatinous; partially opaque, yellow-white and granular, with numerous calcified foci *(right)*.



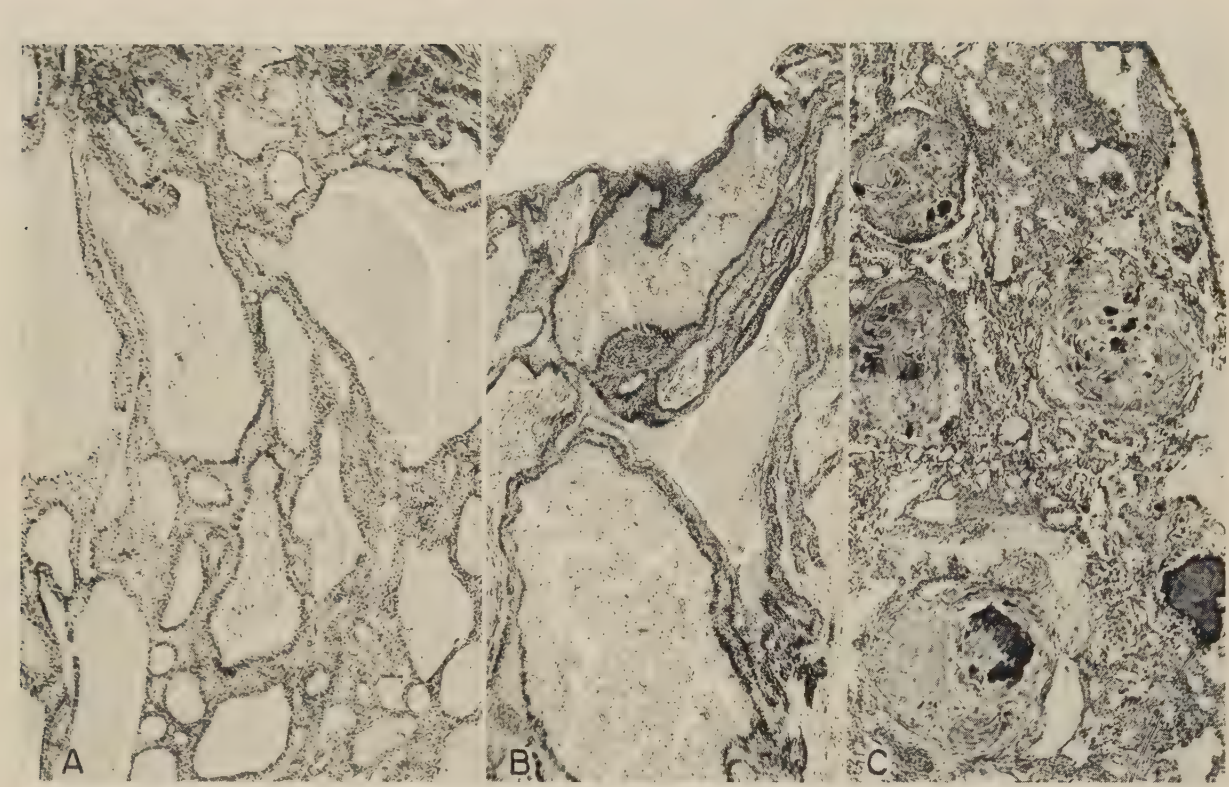
Solid tumor with papillary cystadenomatous pattern and several small cysts, compressing pituitary at right. x6.



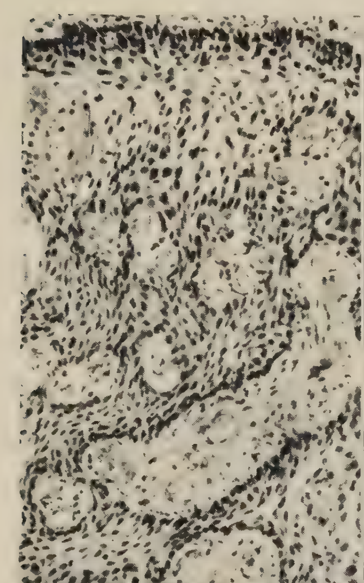
Largely cystic tumor containing gelatinous material and calcific deposits, which were demonstrated in x-rays. x 8.



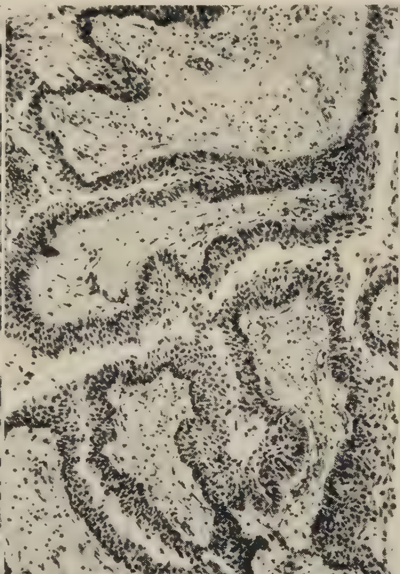
Hyalin-like and keratin-like material in many tumors appears to be produced by the epithelial cells (**A**, x145; **C**, x75). Foreign body giant cell reaction to keratinoid material (**B**, x145). Apparent deposition of mineral salts (**C** and **D**, x125).



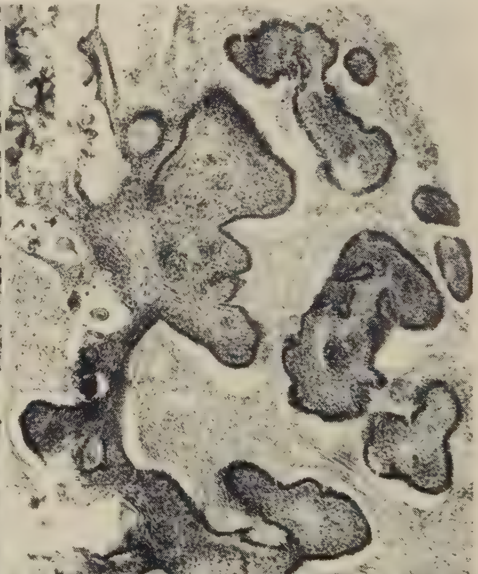
Cystadenomatous and papillary cystadenomatous patterns. A and **B.** Some spaces contain clear homogeneous or granular eosinophilic material; others, numerous lipid-filled histiocytes. Partly cystic tumor. x 62, x 48. **C.** Area in similar tumor with more compact architecture. Epithelium is producing masses of keratin-like or "enamel organ-like" material, which is partially calcified. x 55.



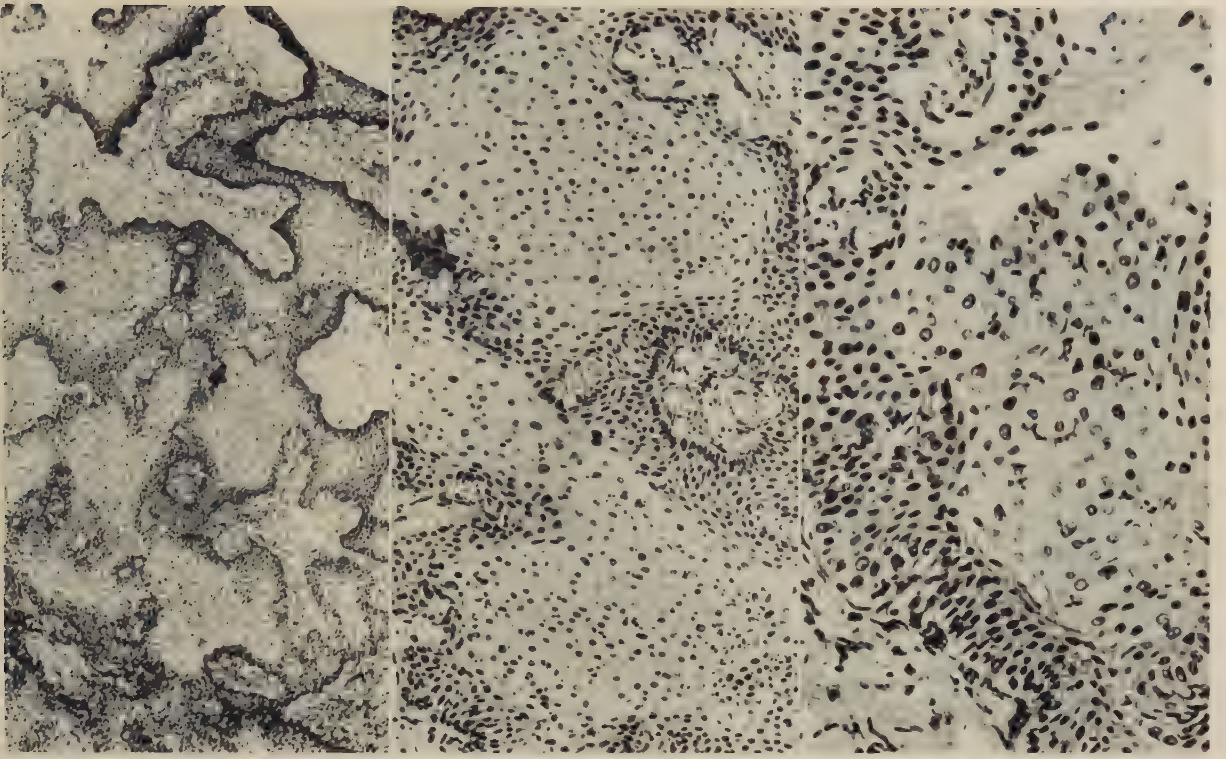
Ameloblastic pattern has been emphasized in the literature. Solid tumor. x 125, x 125.



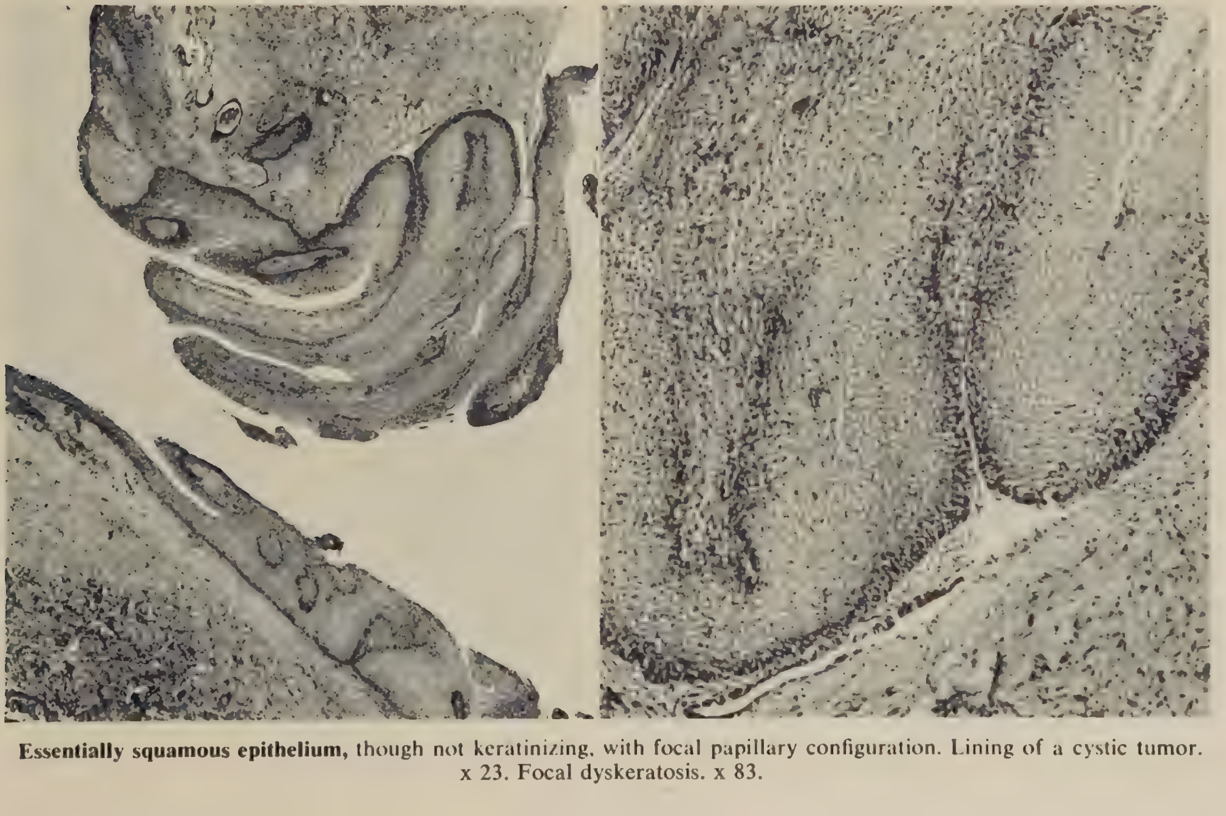
Papillary structure in this case has been produced by separation of mid-portions of solid cell cords. x 90.



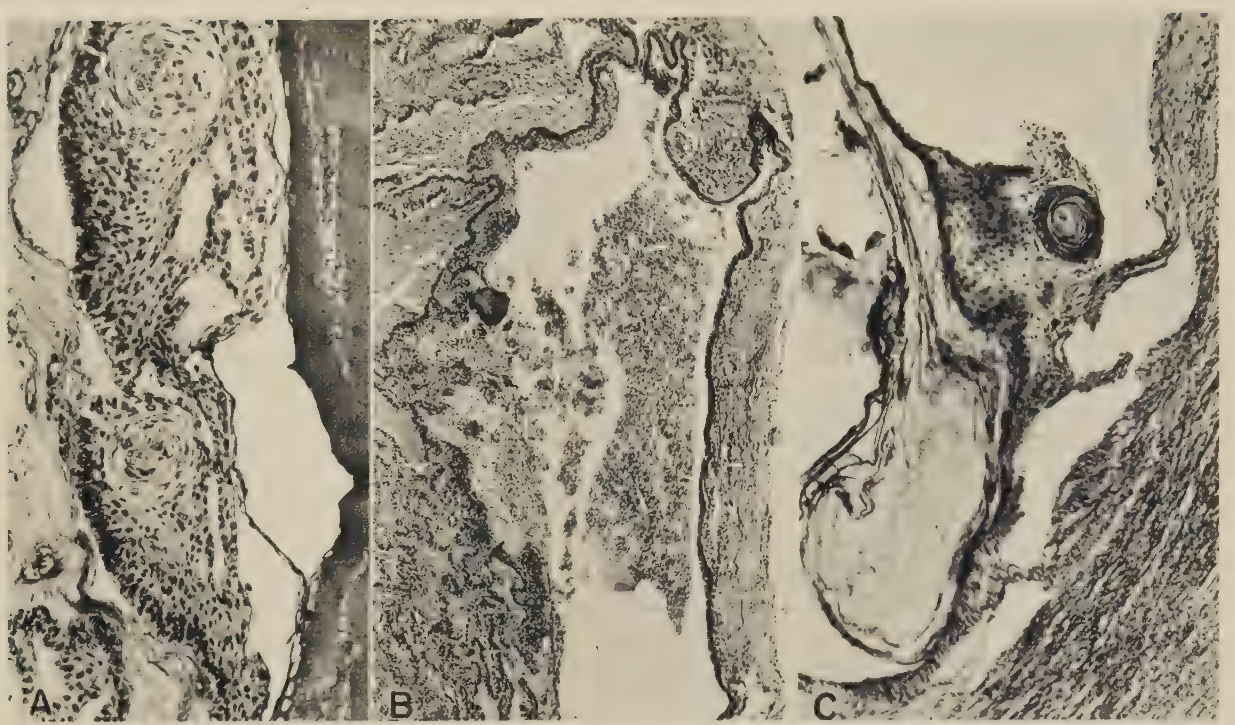
Basaloid pattern. Solid nests similar to basal cell carcinoma with tall palisaded outer layer of cells resembling ameloblasts. x 55.



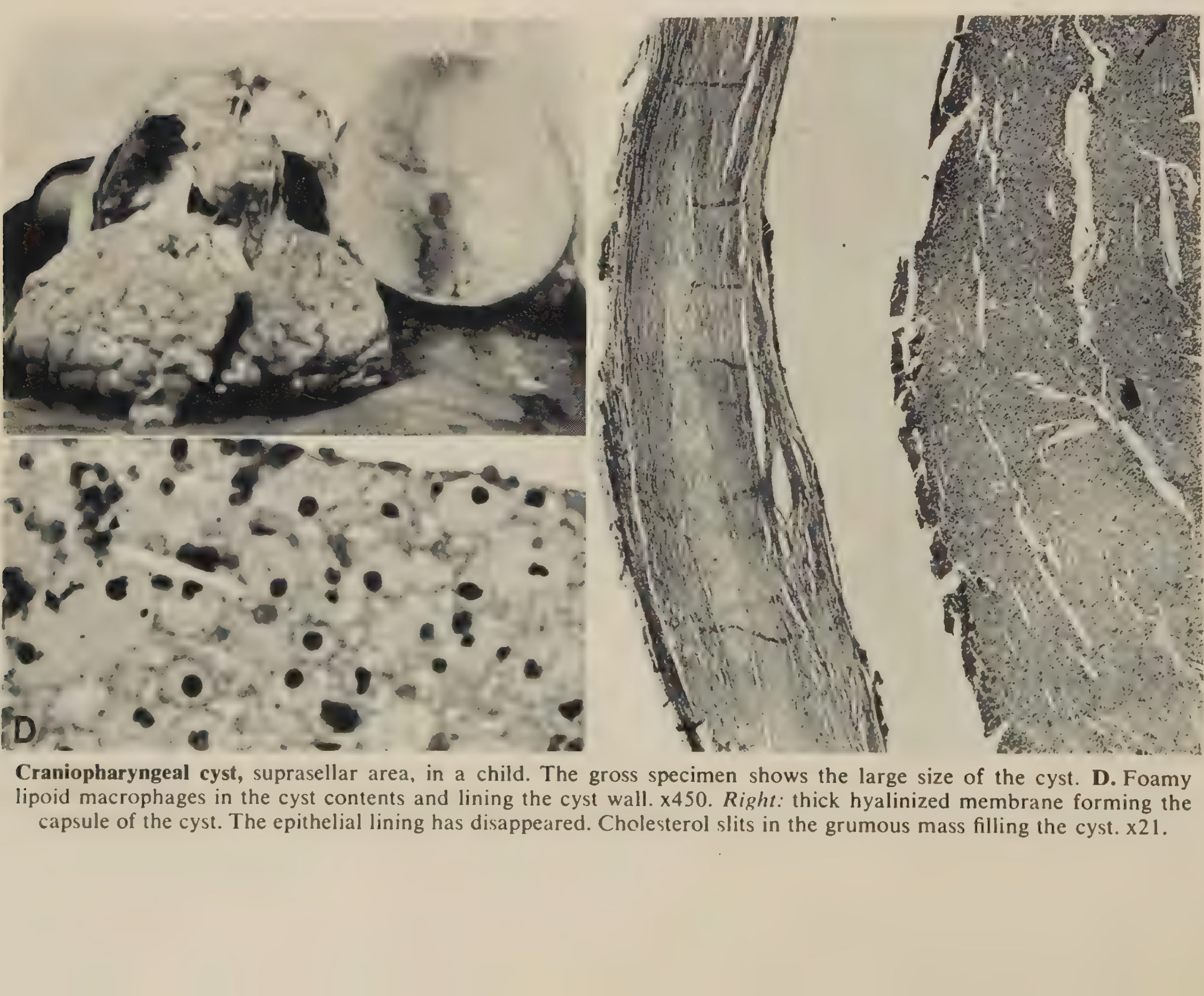
Squamatoid differentiation of proliferating undifferentiated epithelium in largely solid tumor. x 48, x 125. Peripheral undifferentiated cells with hyperchromatic nuclei, central oval and polyhedral cells with pale cytoplasm, no intercellular bridges. x 185.



Essentially squamous epithelium, though not keratinizing, with focal papillary configuration. Lining of a cystic tumor. x 23. Focal dyskeratosis. x 83.



"Craniopharyngiomal" cysts. Craniopharyngiomas may contain small and large epithelium-lined cysts (**B,** x48), or may occur predominantly as a cyst with only focal areas of epithelial proliferation. The epithelium of the cyst may reflect varying potentialities, as do the tumors: **A.** Cyst lining with glandular and ductlike structures. x125. **C.** Keratin-producing squamous epithelium, with biologic behavior of cholesteatoma. x70.



Craniopharyngeal cyst, suprasellar area, in a child. The gross specimen shows the large size of the cyst. **D.** Foamy lipoid macrophages in the cyst contents and lining the cyst wall. x450. *Right:* thick hyalinized membrane forming the capsule of the cyst. The epithelial lining has disappeared. Cholesterol slits in the grumous mass filling the cyst. x21.

CHAPTER 21

MALIGNANT TUMORS OF THE NOSE SINUSES AND PHARYNX

Carcinoma. — About two per cent of all carcinomas develop in the nose and sinuses, and carcinoma is by far the most common malignant tumor of the upper respiratory tract. The predominant type is the transitional cell carcinoma, most frequent in the nose and nasopharynx and, in descending order of frequency, in maxillary, ethmoidal, frontal, and sphenoidal sinuses. The sinuses are often involved by extension of tumors primary in neighboring parts.

Carcinomas arising from the normally squamous epithelium of the nares are either squamous cell or basal cell tumors, and those that arise from leukoplakia and metaplastic epithelium are squamous cell in type.

The carcinomas that originate in the nose, particularly in the turbinates and ethmoidal area, show a greater tendency to squamous cell differentiation than do those arising in the sinuses; however, of eleven tumors of the nasal cavity in the Registry, two were squamous cell, two adenocarcinomas, and seven undifferentiated carcinomas.

Carcinomas arising in the nose and paranasal sinuses show a greater variation in cell type and arrangement than do those from the nasopharynx.

Tumors that are patterned after the mixed tumor of the salivary gland type and after the bronchial adenoma form a group separate from the frank squamous and transitional cell carcinomas and adenocarcinomas. It is these tumors that have the adenoid-cystic pattern of the basal cell tumor arising from hair-follicle epithelium, and that include a mesenchymal component as seen in the mixed tumor. This may vary from a mucinous character to differentiated cartilage. The response of this group is of more than academic importance, for it has been noted that they may metastasize. They tend to have the long, drawn-out clinical history of the mixed tumor and bronchial adenoma. This basaloid type of tumor is much less common in the nasopharynx. It is this type that Willis insists is ameloblastic, arising from paradental epithelial residues. He cites a case from his own experience in which the tumor followed injury to the maxillary sinus from extraction of teeth. While this may apply to an occasional case, it would be more convincing as a generality if the tumors retained the relative benignancy of the ameloblastoma and if there were any other evidence of dental origin in tumors showing the ameloblastic feature.

Carcinomas in the sinuses tend to papillation and the cells either retain their transitional undifferentiated form or become columnar, even to the point of producing mucin. Tumors of the squamous cell type are not uncommon in the maxillary sinus, particularly if they originate in the lower portion of the sinus. Here they are dangerous because of their tendency to invade the alveolus and to metastasize.

The malignant tumors of the nose and paranasal sinuses metastasize less freely than do those of the nasopharynx but they involve large portions of the contiguous tissues by invasion and by pressure atrophy.

It is surprising how frequently dacryocystitis is the first clinical evidence of tumor of the nose or sinuses. This clinical feature places the diagnostic responsibility on the ophthalmologist, for it may lead the patient to consult him first.

Carcinomas of the nasopharynx do not exhibit the striking variation of cell type and architecture that do those of the nose and sinuses. They are seen usually in one of two architectural forms, most commonly of the transitional type of epithelium. In one the cells are palisaded in ribbonlike fascicles associated with a lymphatic tissue component. This is the classic REGAUD TYPE and is the tumor to which the term LYMPHOEPITHELIOMA might most appropriately be applied. The second is the SCHMINCKE TYPE, a diffuse, very cellular tumor without any special arrangement. The cells are more often epithelioid than transitional, are round and polygonal, and are not closely associated with the lymphatic tissue component. The outline of the individual cell is usually vague, but there is more cohesion between the cells than is evident in the reticulum cell sarcoma. This old eponymic classification is not used now, but it is included for its historic interest.

TRANSITIONAL CELL CARCINOMA is the most common tumor of the nasopharynx. Whiteleather has reported sixteen cases, emphasizing the clinical aspects. The tumor usually originates as a small flat nodule in the region of the eustachian tube orifice, from which it spreads widely beneath the mucosa without ulceration. Occasionally the tumor is polypoid. It is possible for transitional cell carcinoma to extend by continuity of structure through the eustachian tube into the middle ear. The great wing of the sphenoid may be invaded and the cranial nerves directly involved, giving rise to clinical symptoms that may be misleading. Involvement of the eustachian tube is apparently the most frequent cause of the earliest symptoms, especially a feeling of blockage in the ear, and the patient is often subjected to considerable irrelevant treatment before the tumor is recognized. This likelihood has been reduced, of course, by widespread routine use of the nasopharyngoscope. Involvement of the lateral retropharyngeal lymph nodes is usually the next sign to appear. The nodes can be palpated just behind the angle of the jaw. Later the deep cervical chain along the anterior border of the sternocleidomastoid muscle is invaded. Trotter was the first to point out this feature and to call attention to the fact that were it not for the lymph-node signal, the pharyngeal tumor might not be discovered until there was widespread invasion of the nasopharyngeal wall and even extension into the cranial cavity.

The average age of patients with nasopharyngeal carcinoma is younger than that of those with similar tumors of the nose and sinuses. There is some relation between age and type of growth. The pure lymphoepithelial tumors generally occur earlier than those of the differentiated squamous cell. Nasopharyngeal carcinoma is definitely more common in males and it seems to have a particular predilection for Orientals. Of forty-nine cases of carcinoma of the nasopharynx in the Registry analyzed recently, forty-four were of males, five of females. The ages ranged from 20 to 69 years, and twenty-one of the patients were under 30 years of age. In twenty of the cases enlarged cervical lymph nodes were the first evidence of tumor. In one case three years elapsed between the appearance of the lymph-node involvement and the discovery of the primary tumor in the nasopharynx. In another instance the primary tumor was not found until autopsy.

The tumors arise most commonly in or near the fossa of Rosenmüller, and for this reason they have been referred to as peritubular carcinomas. The orifice of a eustachian tube may be occluded early and symptoms referable to the ear can then be the initial clinical feature. They may arise in other portions of the nasopharynx, including the tonsils, but they are rare in the hypopharynx. Pharyngeal carcinomas developing below the level of the palate are practically always frankly squamous in type.

Not all carcinomas of the pharynx are of the transitional cell variety. Of forty-nine cases in the Registry, thirteen were well differentiated squamous cell tumors, although foci of transitional cell or even less differentiated cell types were seen in some. Variation in cell type in different tumors and in portions of the same tumor is characteristic, but this variation is not so prominent as it is in tumors of the nose and sinuses. It is the experience of the Registry that primary epidermal cell carcinoma is comparatively rare in the nasopharynx and that such differentiation usually occurs in extensions or metastases of the lymphoepithelial (transitional cell) tumor.

The practical lesson is clear. The discovery of malignant epithelial tumor in a cervical lymph node in a young adult, particularly a male, in whom a primary tumor is not obvious, places the burden on the otolaryngologist, who must discover it by careful search of the nasopharynx, especially the fossa of Rosenmüller.

Surgical removal of the primary tumor is obviously impossible and the only recourse in the early stage before invasion or metastasis is irradiation. Unfortunately the primary tumor is seldom recognized sufficiently early for successful treatment.

Whatever the terminology used or whatever opinion as to histogenesis be accepted, carcinomas arising from the respiratory epithelium have certain specific clinical and histologic peculiarities. In spite of their aggressive local behavior, the incidence of distant metastasis is much lower in those from the nose and paranasal sinuses than in carcinomas from other sources—breast, prostate, etc., and those in the nasopharynx occur in a younger age group than do most other carcinomas. Since there are further clinical and pathologic features of tumors arising in the nose and paranasal sinuses which differ from those of carcinomas arising in the nasopharyngeal mucosa, it would seem desirable to adopt a terminology that would connote these important differences and to drop the certainly ambiguous term "transitional-cell carcinoma." There is some significance to the term lymphoepithelial carcinoma if, as stated above, it would be restricted to tumors arising from this histologic type of mucosa, particularly from the nasopharynx. The differentiation histogenetically, histologically, and clinically is clearly made by the terms SCHNEIDERIAN CARCINOMA and NASOPHARYNGEAL CARCINOMA, the former applied to carcinomas of the nose and paranasal sinuses, and the latter to those arising from lymphoepithelium.

Adenocarcinoma does not occur commonly in the upper respiratory tract, but a small percentage arising in the nose and paranasal sinuses, and especially in the ethmoidal region, are made up of mucous gland elements, some of them showing papillary architecture and more or less mucous activity. They grow more slowly than the other types of carcinoma in this region. Histologically, they may show characteristics of a malignant tumor and be so diagnosed by the pathologist, but they rarely metastasize. Clinically they are malignant in that they fill the bony cavities, invade the tissues, and, in addition, by pressure atrophy destroy tissues and eventually involve the bones of the face and head and invade the orbit and the cranial cavity. They are not as sensitive to irradiation as the less differentiated epithelial cell tumors. Another feature that makes them particularly serious is that they may not be evident clinically until they have filled a sinus cavity and damaged its wall.

Nonepithelial malignant tumors in the upper respiratory tract are rare, and the majority of these have their origin in the bony or cartilaginous elements. OSTEOGENIC SARCOMA is most common as an invasion from the maxilla. A more myxoid type of sarcoma develops in fibrous or cartilaginous tissues of the very young, particularly in the nasal septum.

PRIMARY MALIGNANT MELANOMA occasionally arises in the nasal and sinus mucosa. In a recent study of malignant melanomas, Allen and Spitz include eight in the nasal cavity and two in the paranasal sinuses. They mention particularly the grave prognosis of the melanomas occurring on the mucosae.

EXTRAMEDULLARY PLASMACYTOMA is a true tumor, but at times is difficult to differentiate from an inflammatory lesion in which there is a high concentration of plasma cells. Like its closely related syndrome, intramedullary multiple myeloma, it occurs most commonly in the male but is not so definitely restricted to the older age group. Geschickter reported a plasmacytoma in the nasopharynx with multiple bone involvement in an 18-year-old boy. It most frequently arises in the soft tissues of the pharynx, palate and nose, although it has been reported in other parts of the respiratory tract including the mucosa of the sinuses, the tongue, and the subcutaneous tissues of the head. One example, primary in the thyroid, was received recently by the Registry.

It manifests itself clinically as a diffuse swelling, but occasionally it is pedunculated. There is no distinguishing clinical characteristic, however, nor in the early stages is there any constitutional reaction. Bence-Jones proteinuria, which is a characteristic of the intramedullary tumor, does not occur unless the latter is a complication. When the diagnosis has been established, a roentgenologic survey of the skeleton should be made to determine the presence of bone tumor.

The relationship between the extramedullary tumor and the multiple syndrome is not clear. Figi, Broders and Havens, reporting on the cases accumulated at the Mayo Clinic, stated that a large percentage of the extramedullary cases eventuate in bone involvement. They emphasized the discouraging feature that bone tumors may become evident years later even if the local lesion is eradicated. Generally the extramedullary tumor does not have the hopeless implication that is carried by the myeloma of the bone, even though it will metastasize to local lymph nodes. Neither the intramedullary nor extramedullary tumor is particularly sensitive to irradiation.

Under the low power of the microscope the plasma cell character of the tumor can be recognized, but on greater magnification the neoplastic features of the cells become obvious. There are numerous multinucleated cells and the nuclei do not have the uniform cartwheel characteristics. The cell has a greater proportion of cytoplasm than the inflammatory plasma cell and it is less basophilic in its staining. Furthermore, the cells have a little more cohesiveness than the inflammatory prototype, and mitotic figures can be found. These are not present in the plasma cells of exudate.

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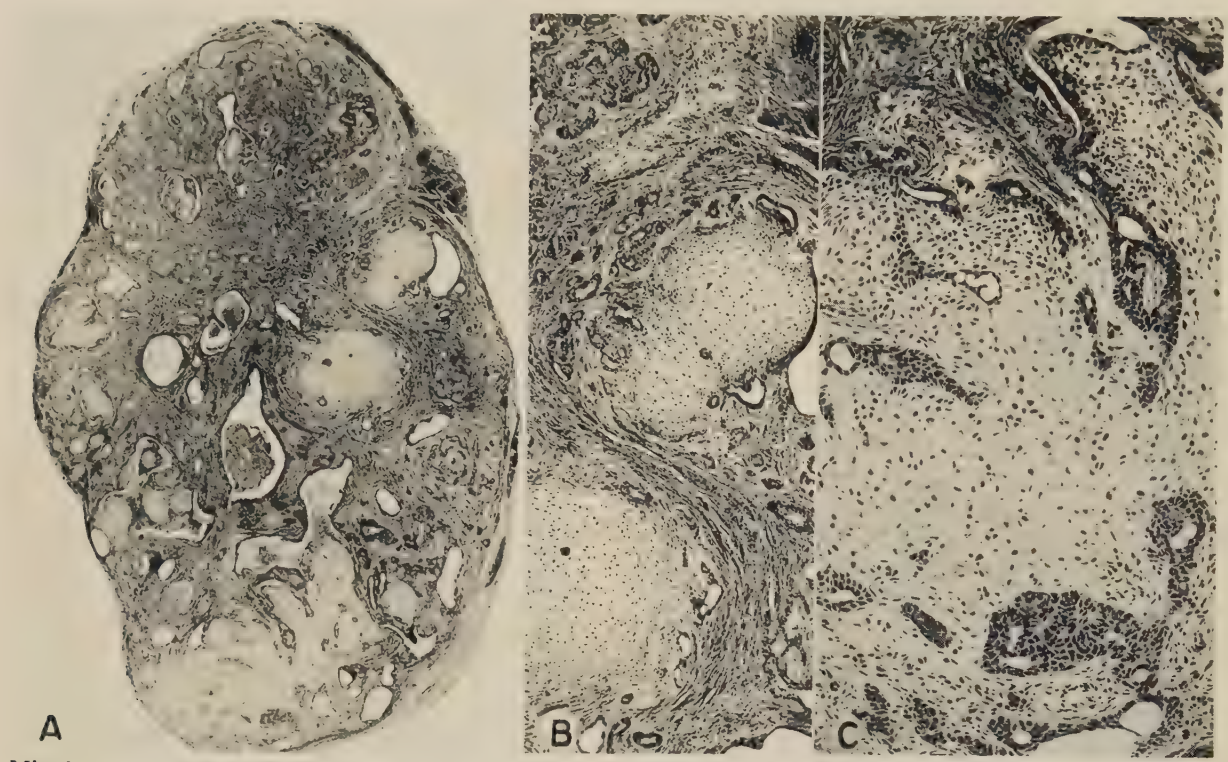
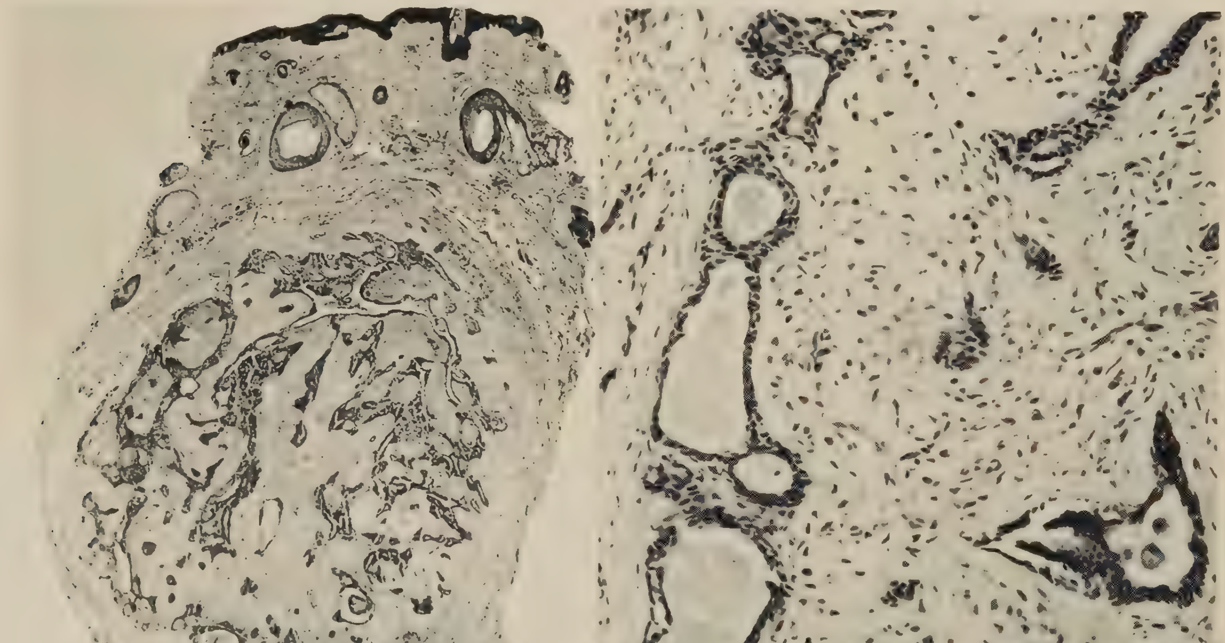
BENIGN "MIXED TUMORS," SKIN OF NOSE

(SYRINGADENOMA)



Mixed tumor of salivary gland type, skin of nose, of dermal (sweat) gland origin. **A.** Well circumscribed mass, showing mixture of epithelial and mesenchyme-like elements: proliferating glandular structures, some showing cystic dilatation, and focal pale areas which resemble cartilage. x23. **B.** Proliferating tubules surrounding and blending with chondroid foci. x35. **C.** Transition zones between proliferating epithelial element and its myxochondroid product. x90.

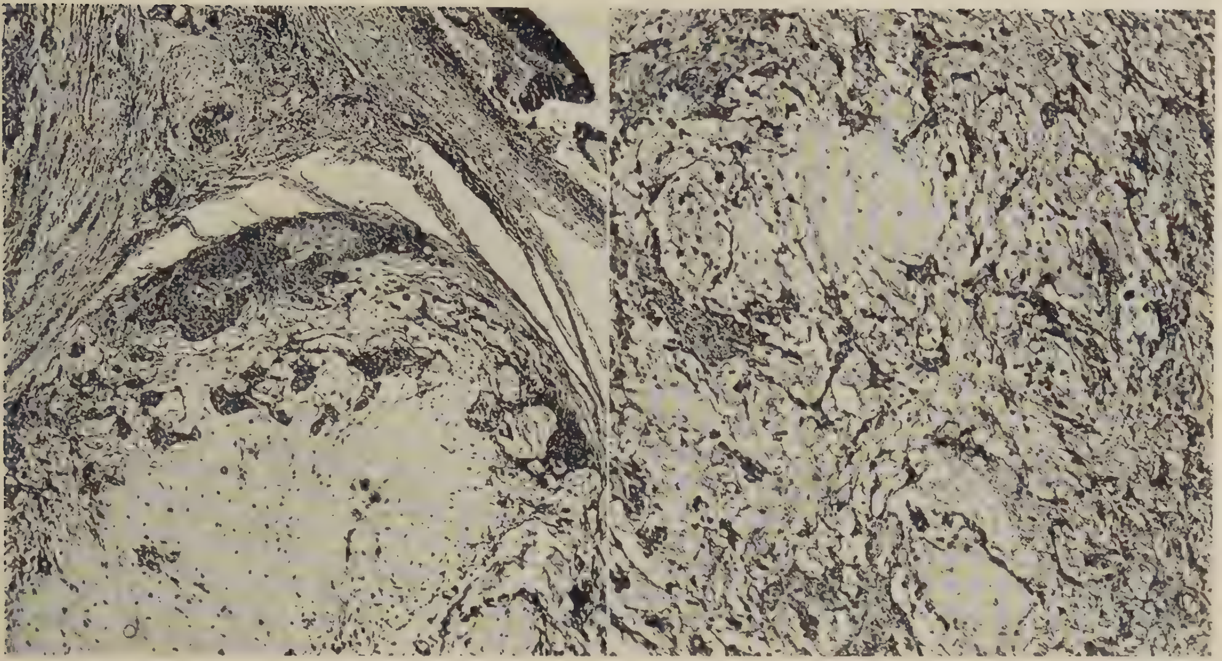


Mixed tumor, tip of nose of a 38 year old man. Touched with an electric needle in the belief it was an infected follicle, it grew to 1 cm. in three weeks (**D**, x21). **E.** Cells extending from epithelial tubules and nests, becoming spindle and stellate in the myxoid component. Evidence of cellular secretion within and outside of glandular structures. x145. (South Bend Medical Foundation, Ind.)

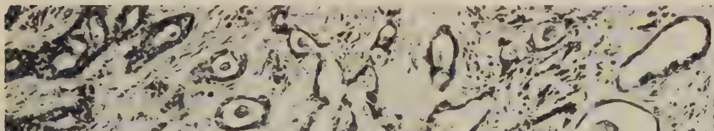
Tumors of the upper respiratory tract which are analogous to those commonly occurring in MAJOR salivary glands are shown on this and the following 11 plates.

BENIGN MIXED TUMOR

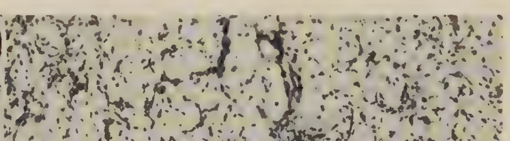
(POLYMORPHOUS ADENOMA)



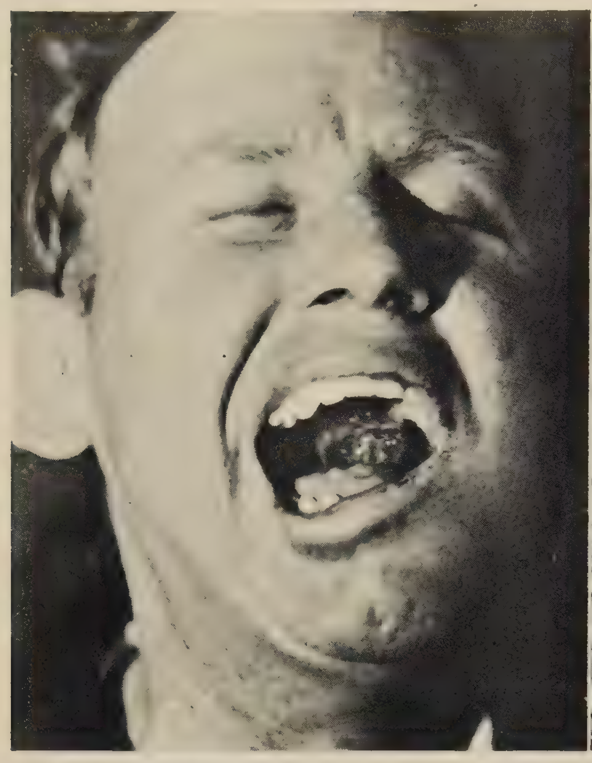
Mixed tumor in nasal septum of a 20 year old man. Large obstructive mass removed. No recurrence several months later. Within and adjacent to mucinous and chondroid areas are islands and clusters of small round epithelial cells with little tendency to acinar arrangement; and delicate anastomosing and branching strands of cells, as well as individual cells, which are stellate and spindle shaped. Partial encapsulation. x48, x75.



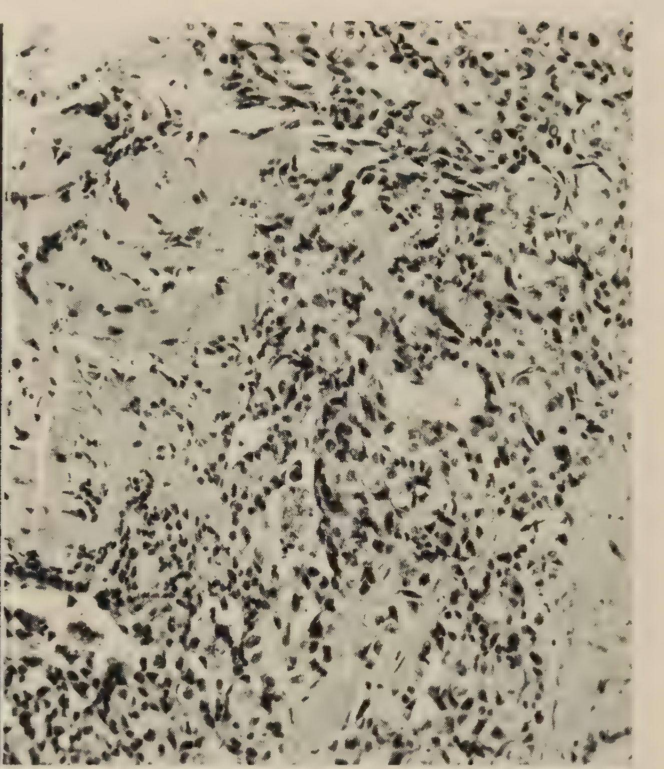
Mixed tumor, nasal septum of a 57 year old man, gradualy enlarging since partial removal 40 years previously. At that time, growth caused nasal obstruction. Predominant epithelial element with varied glandular and tubular pattern in fibromyxoid stroma. x75, x125.



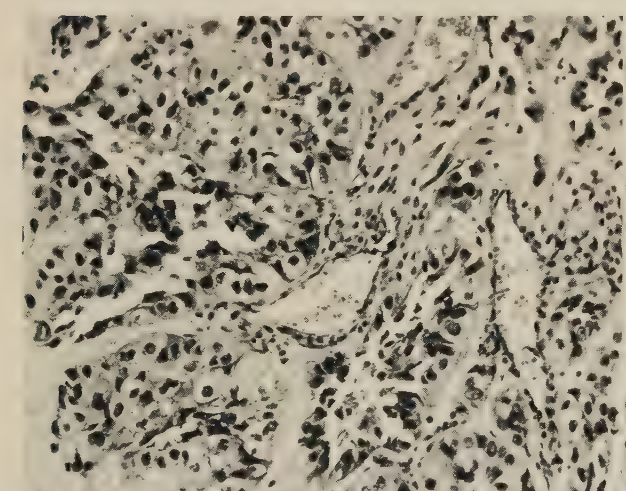
Mass (8x4 cm.) **in lateral pharyngeal wall** of a 55 year old woman, appeared several years after removal of parotid tumor. Myxomatoid areas, and solid masses and strands of spindle-shaped epithelial cells. x100. (L. Schall, Boston.)



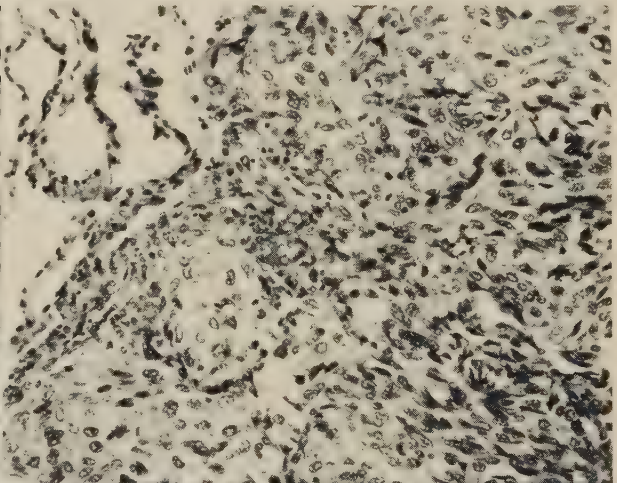
Malignant mixed tumor of pharynx as it appeared after recurrence.



Origin in mixed tumor of salivary gland type is suggested by hyalin focus (above) within otherwise cellular carcinoma. x 145.



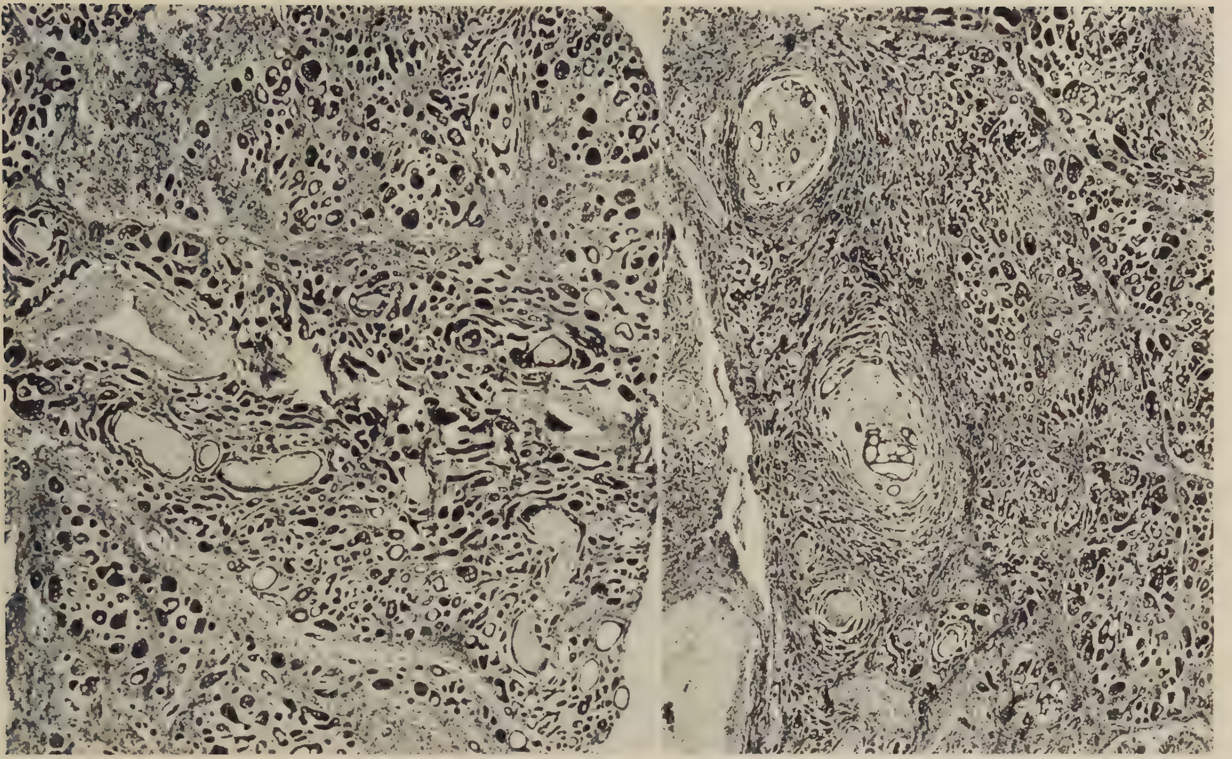
The recurrent tumor. Though most areas were poorly differentiated, occasional fields contained poorly formed glandular elements with large, frequently clear cells. x 148.



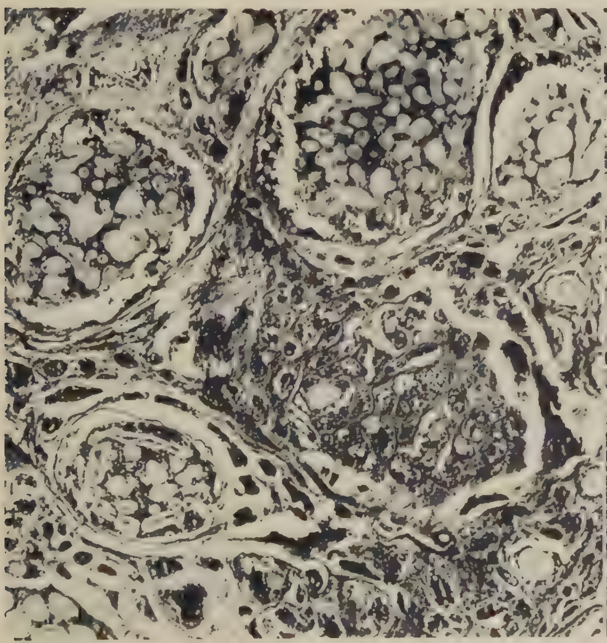
Lung metastasis with spindle cells, squamatoid epithelium and no stromal component. Several brightly mucicarmine-positive globules demonstrated in this area. x 145.

ADENOID CYSTIC CARCINOMA

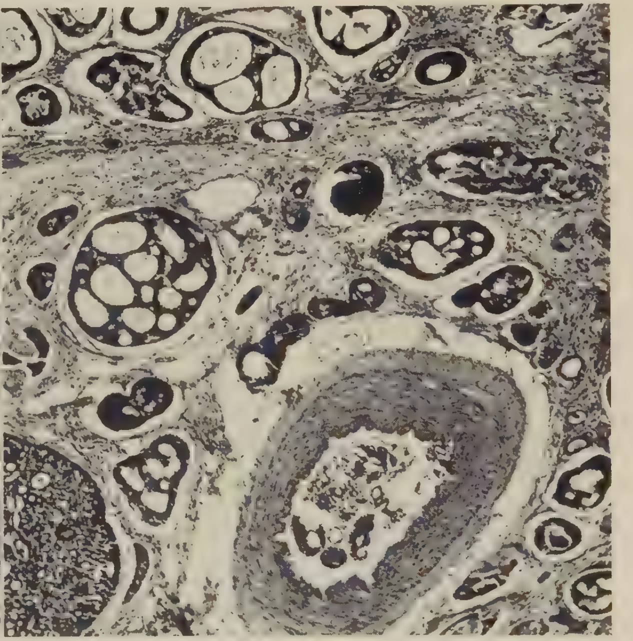
(ADENOCARCINOMA, CYLINDROMATOUS TYPE)



Histologic features of adenoid cystic carcinoma at very low magnification. Circumscribed masses, cords and tubules of deeply stained cells, solid or with large and small cystic spaces. Note extensive permeation of perineural lymphatics, a common feature; also invasion of nerve itself (right) and perivascular lymphatics (left). Both x 25. A specific tumor of major salivary gland which may also arise in all parts of the upper gastrointestinal and the respiratory tracts, though extremely rare in sites such as larynx and esophagus.



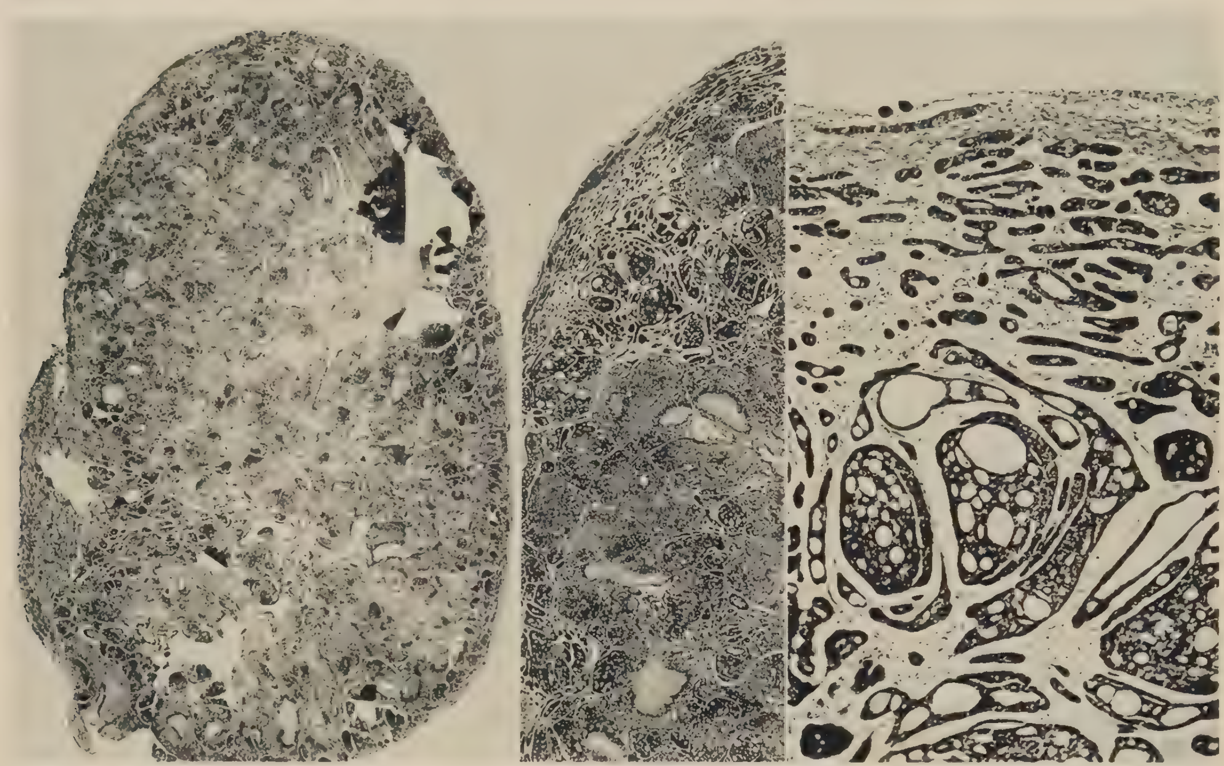
Cylindromatous element. Hyalinizing and hyaline material rather than mucinous secretion within the cystic spaces explains the designation cylindromatous carcinoma ("cylindroma"), which some prefer. These may branch, fuse, surround and isolate groups and strands of epithelial cells. x 70.



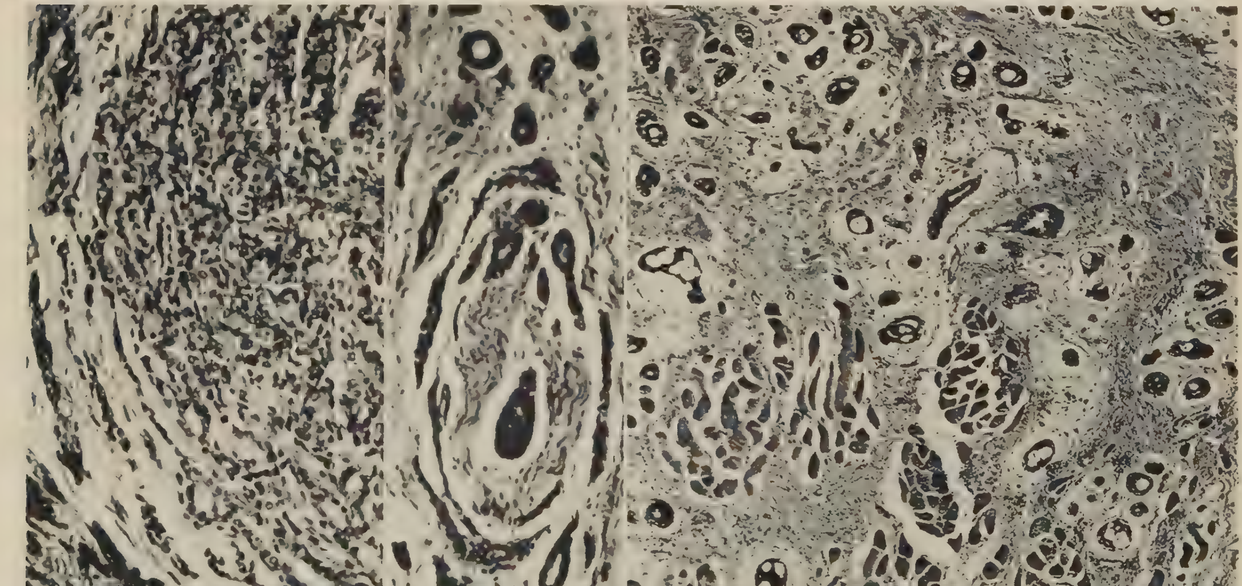
Tumors with similar histologic structure occur in other organs such as lacrimal gland, breast, female genital tract, and skin. This field is from a tumor in the region of Bartholin's gland. x 70.

ADENOID CYSTIC CARCINOMA

(CYLINDROMA, ADENOMA, BASALOID "MIXED TUMOR")



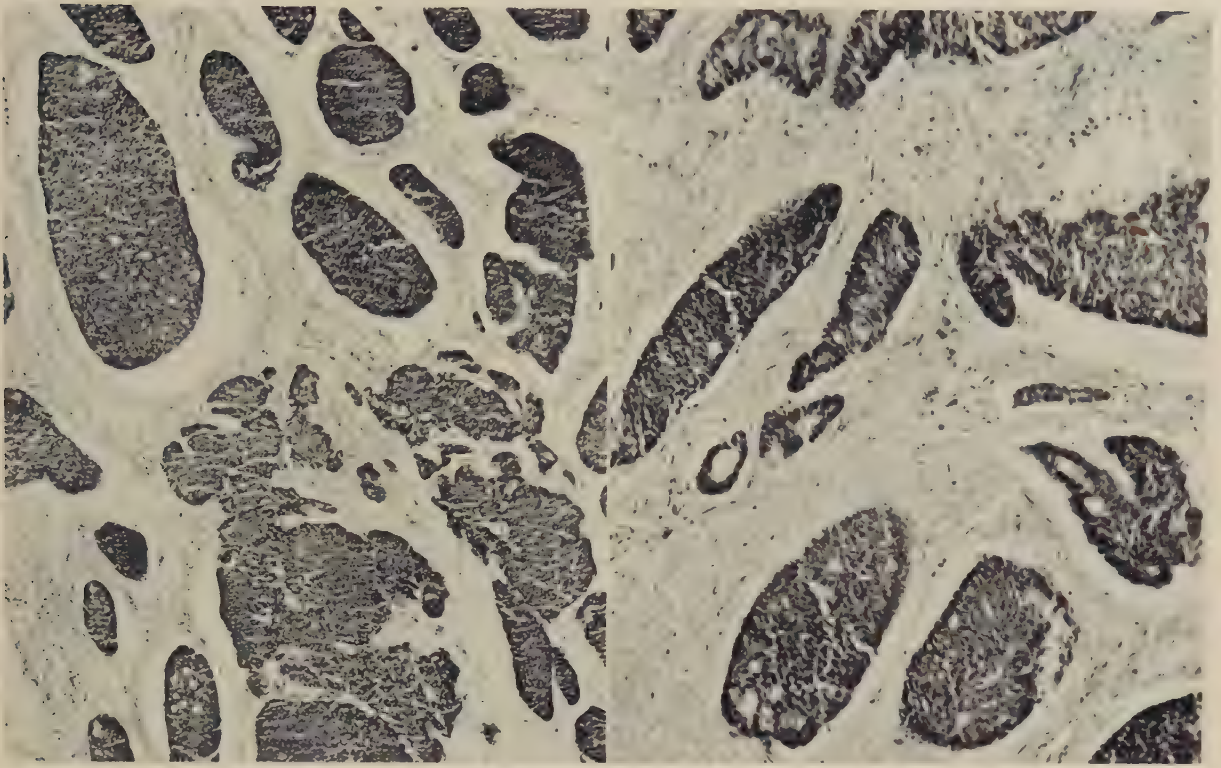
Polypoid portion of mass in nasal cavity from primary tumor filling left antrum, eroding bone and also extending to canine fossa. Nasal "polyps" previously excised. Local resection in 54 year old man with clinical symptoms of 2 years' duration. Cellular tumor with sharply defined tubular and duct-like structures and well-circumscribed larger masses. Within these, cystic spaces of varying size contain mucicarminophilic secretion. x 6, x 10, x 55. Three year later, blind left eye; extensive local recurrence (below); extension to base of brain; metastatic lesions throughout both lung fields in chest x-rays.



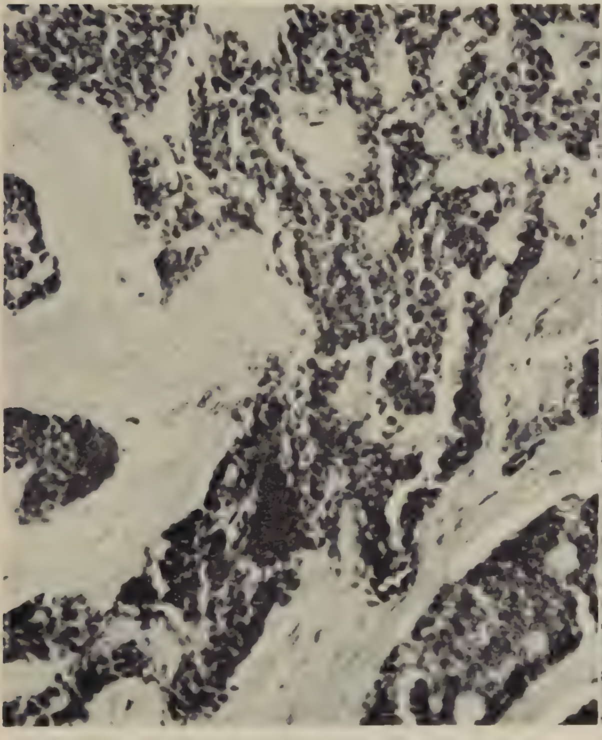
Recurrent tumor in multiple sites demonstrated in 8 of 10 biopsy specimens from same patient. Histologic pattern similar to primary tumor. *Left,* more solid cellular area in floor of orbit. x 205. *Center,* perineural lymphatic invasion, present in biopsies from orbit, cheek, and lateral aspect of nose. x 125. *Right,* invasion of striated muscle. x 62.

ADENOID CYSTIC CARCINOMA, SPHENOID SINUS

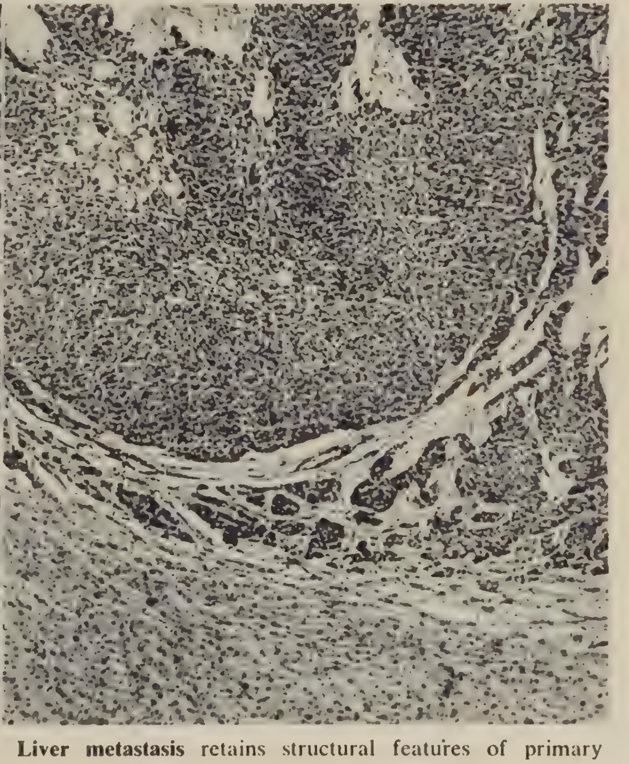
(SOLID VARIANT)



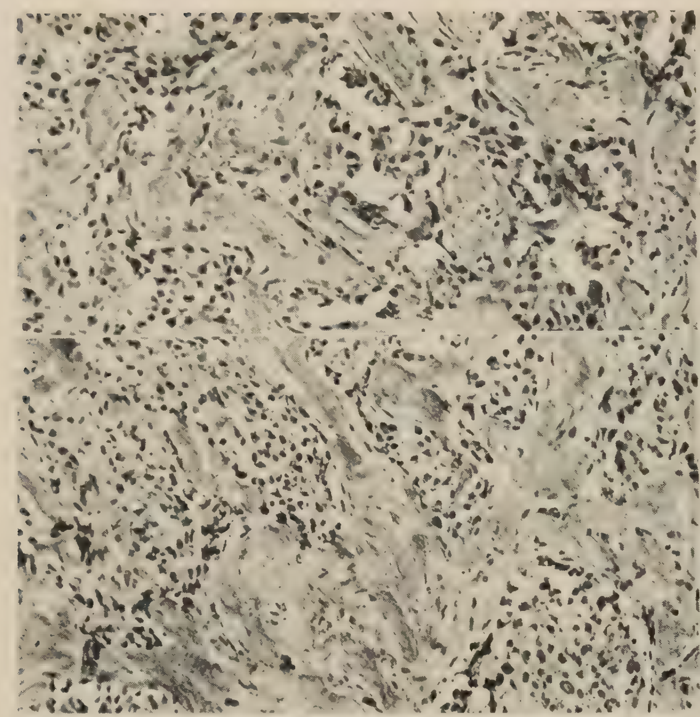
Tumor in region of sphenoid sinus in a 60 year old colored male of unknown duration, which destroyed body and left wings of sphenoid bone and extended to overlying dura and into left orbit causing propstosis on left. Nasopharynx not examined. Circumscribed masses of cells with only few cystic spaces and few tubular groupings. x 70, x 125.



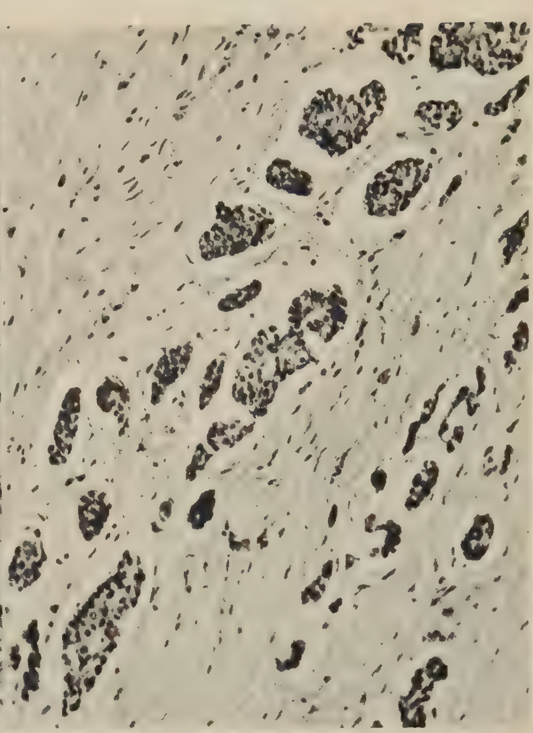
Uniform oval hyperchromatic cells with little cytoplasm and loose relatively accelular stroma. x 275.



Liver metastasis retains structural features of primary tumor. No other distant metastases demonstrated. x 83.

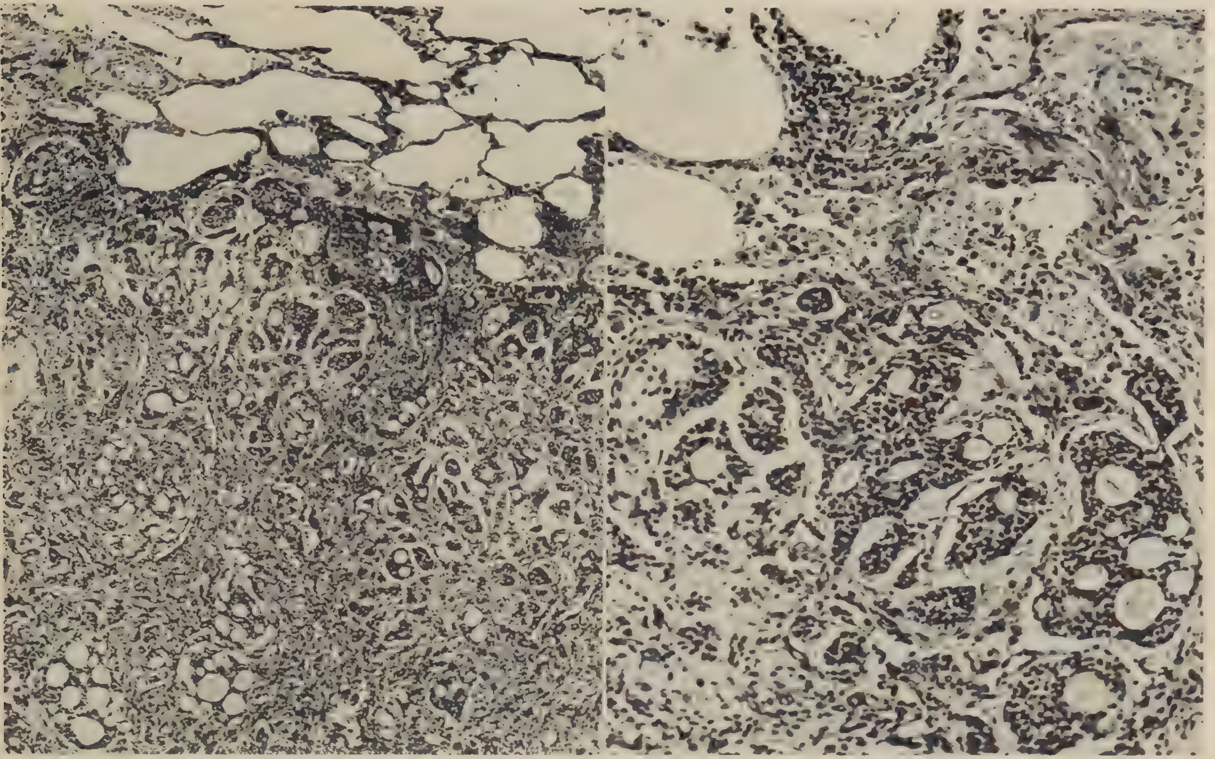


Distorted biopsy specimen of firm yellowish tumor on left Eustachian cushion diagnosed transitional cell carcinoma. Both x 165. Forty-four-year-old man with intractable left facial and supraorbital pain of 6 months' duration. Osteolytic lesion medial to petrous apex, in skull x-rays.

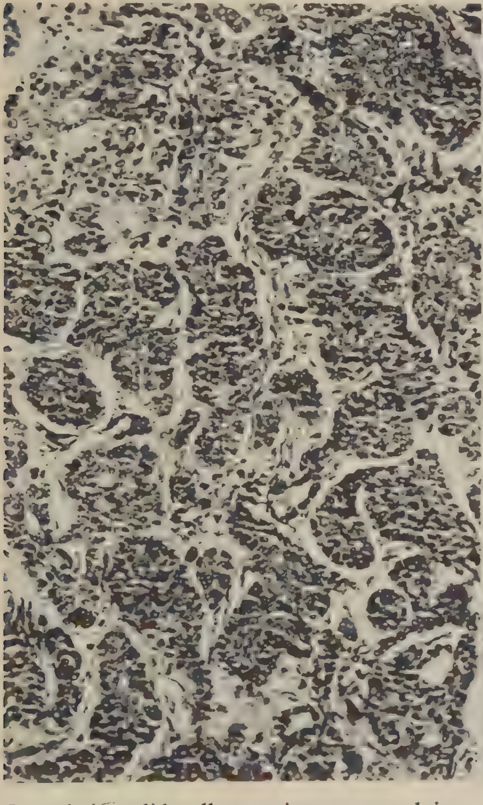


Postmortem nasopharyngeal specimen from previously irradiated tumor which extended through foramen lacerum. Typical adenoid cystic pattern. x 125.

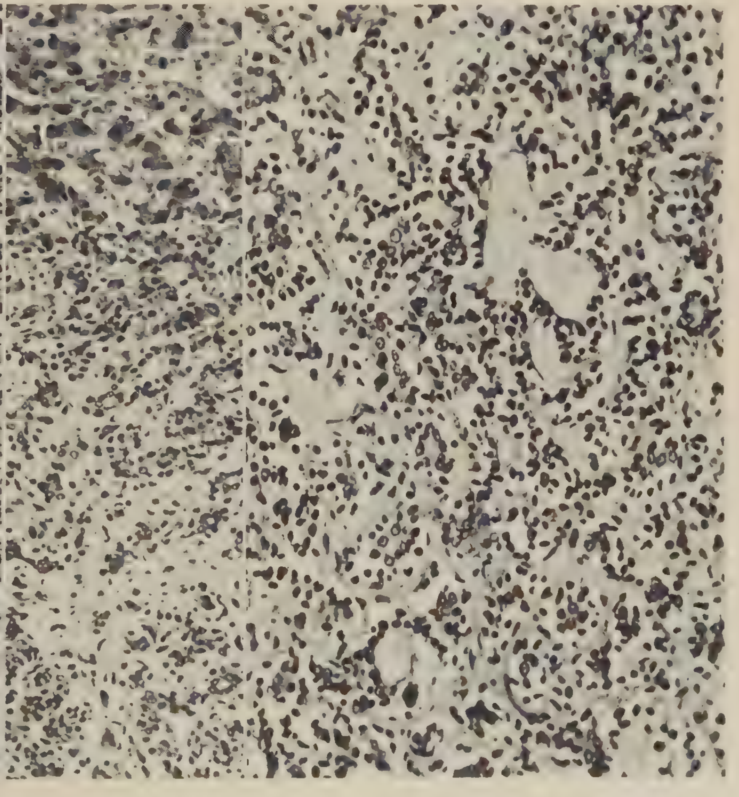
Multiple metastatic tumor nodules (at autopsy) in soft palate, cervical lymph nodes, kidneys, lungs and pleura, liver (see next plate). Both **kidneys** contained numerous solid nodules, the largest 2.5 cm. in diameter. These fields show the well differentiated adenoid cystic structure with mucicarminophilic cystic spaces and strands of intercellular material. x 70, x 145.



Lung metastasis from tumor shown on previous plate. Mucicarminophilic material within cystic spaces and between cords, nests and strands of epithelial cells simulating mixed tumor. x 48, x 125. Each lung contained numerous metastatic nodules, the largest 2 cms. in diameter.



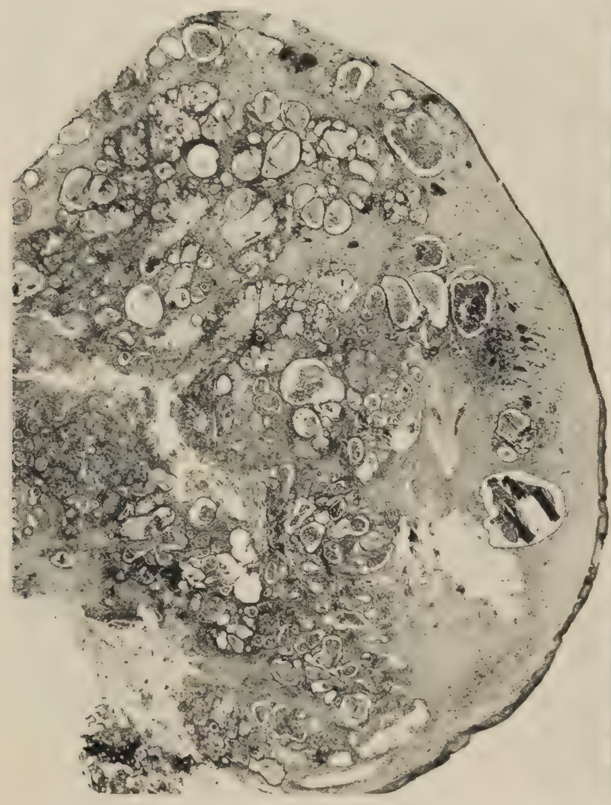
Growth in solid cell groupings occurred in all other fields of same lung metastasis at pleural surface. x 145.



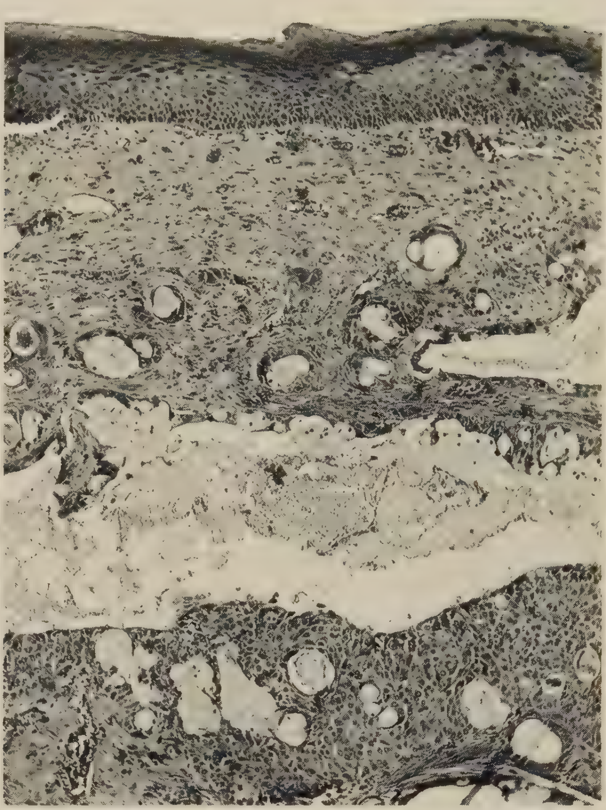
Liver metastasis with predominant cylindroid pattern. Anastamosing, irregular strands of material around and between cell groupings were both strongly and weakly positive in mucicarmine stains. x 145, x 275.

MUCOEPIDERMOID CARCINOMA

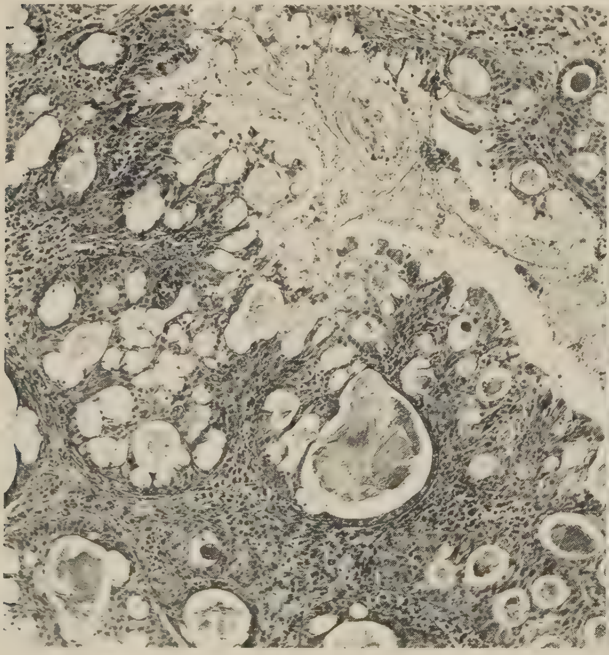
("LOW GRADE MALIGNANCY")



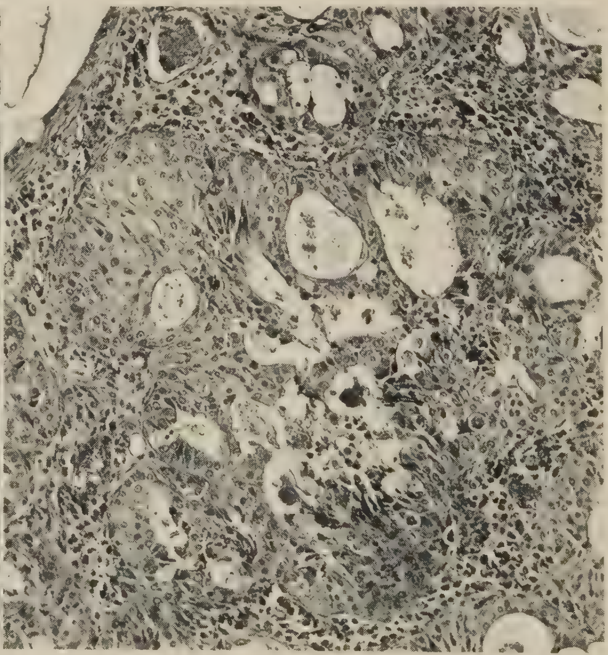
Mucoepidermoid carcinoma, nasal cavity, arising as a polypoid but sessile mass. Squamous metaplasia of uninvolved surface epithelium; no normal ducts or glands. Tumor extends to resected margin; reported erosion of bone. x9.



Ductal origin (as described by Stewart et al.) appears evident in this tumor. Large subepithelial duct shows largely mucus-secreting cells in upper wall; predominantly metaplastic epidermoid element in lower. x75.

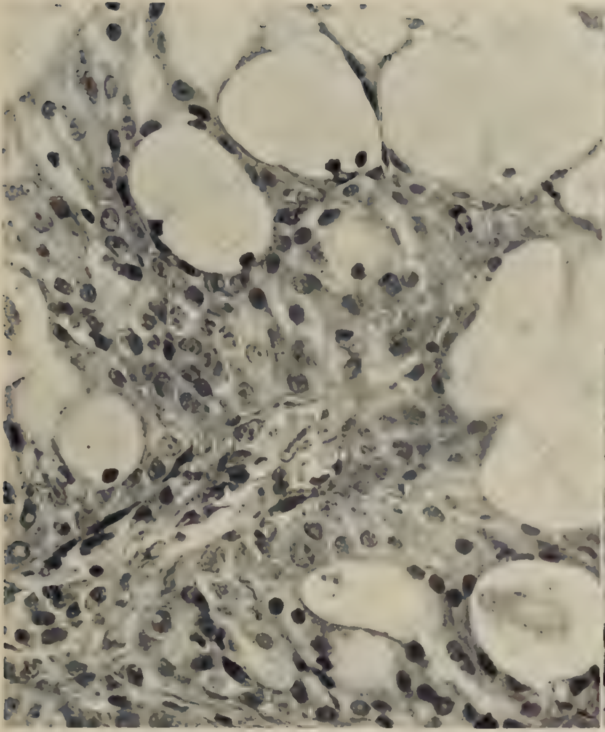


The mucus-secreting element dominates this field, as well as most of the mass. x75. (I.M. Shevick, Hollywood, Calif.)

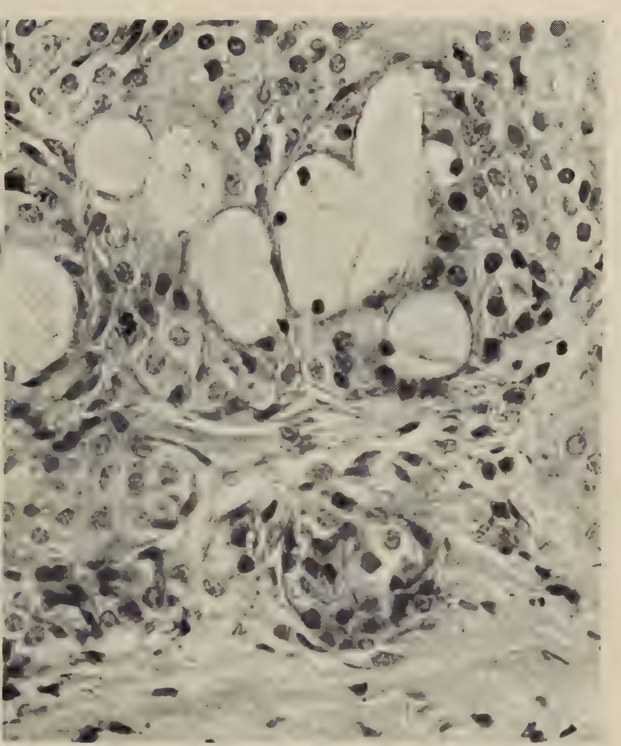


Metaplastic epidermoid component is prominent. Some "transitional" or "intermediate" cell types at bottom.

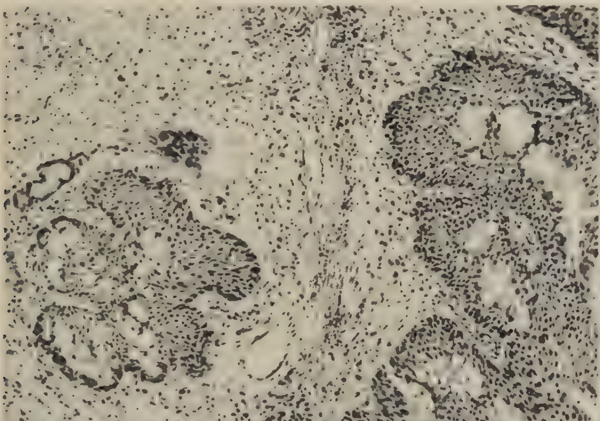
Details from case of previous plate:



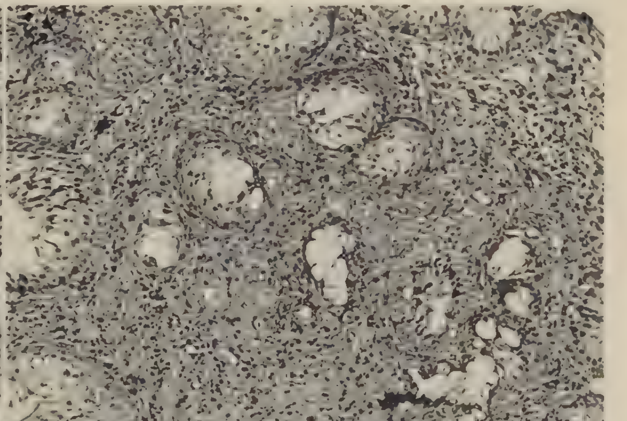
"Double metaplasia": mucus-containing cells and squamous cells. Several mitotic figures. x 395.



Penetration of stroma by peripheral nests and strands of cells. Some undifferentiated cells. x 395.



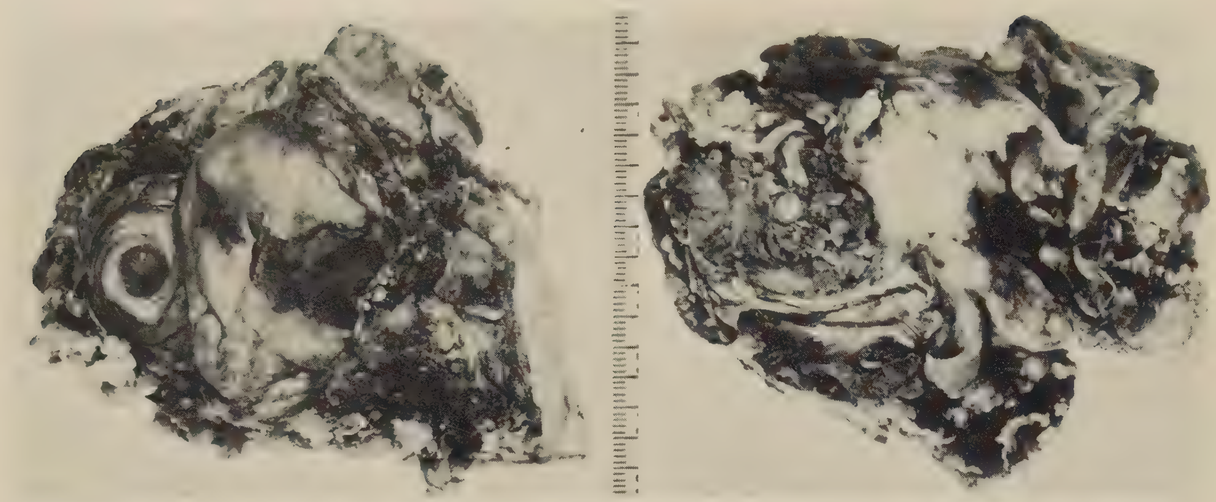
Hyperplasia and metaplasia (benign) of epithelium of surface and a large duct, from nasal cavity of another patient. x 150.



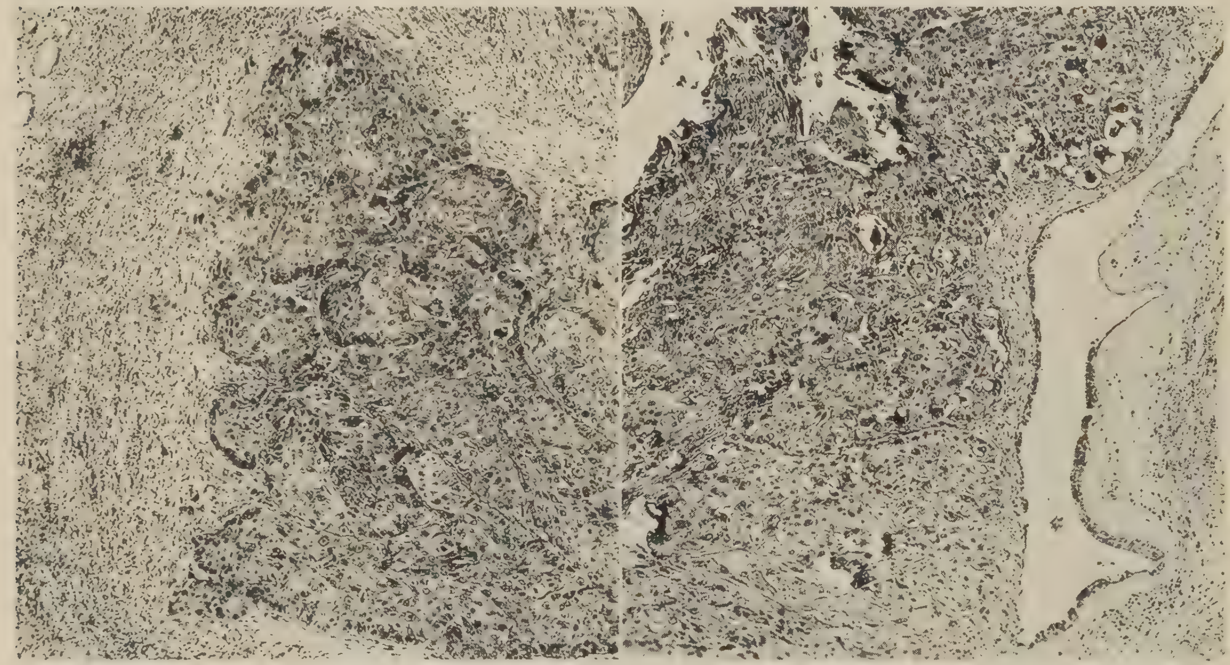
Metaplastic epidermization of mucosa of ethmoid sinus, involving surface and ductal epithelium, from a sinus tract into the ethmoid cells of a 57-year-old man. x 150.

MUCOEPIDERMOID CARCINOMA

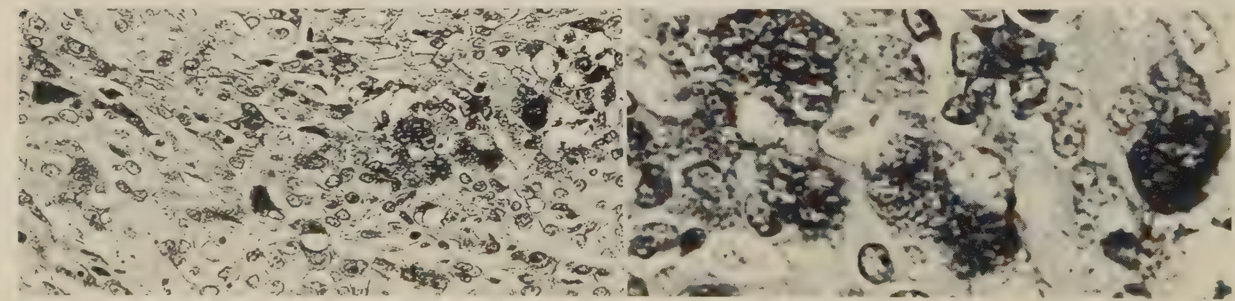
("HIGH-GRADE MALIGNANCY")



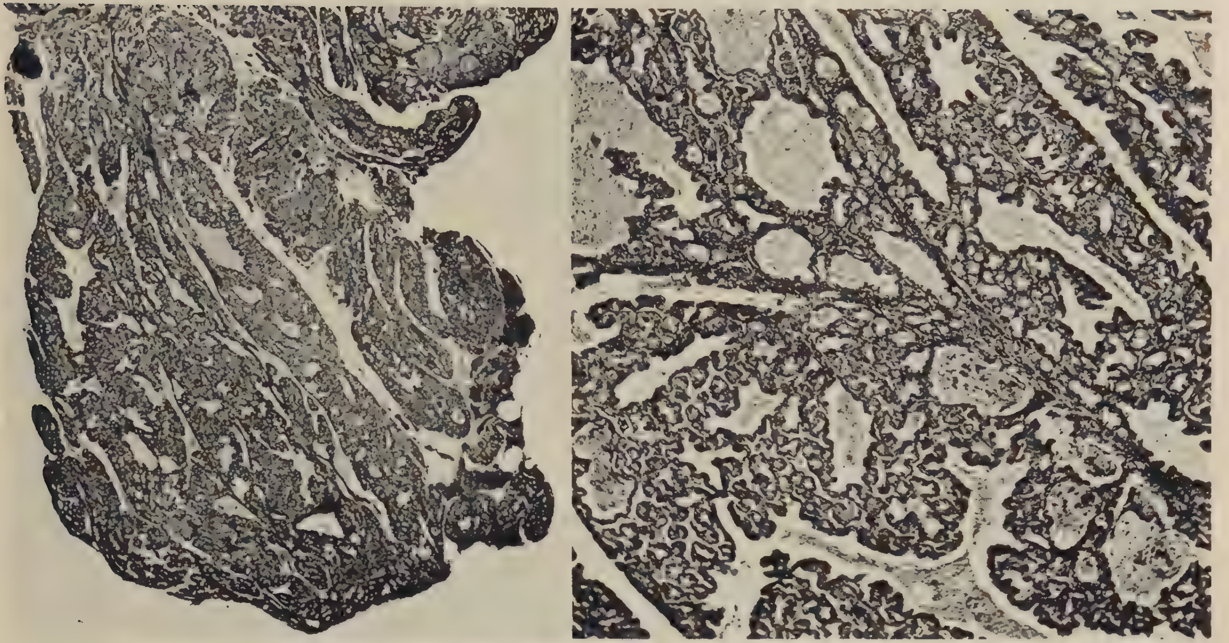
Gross specimen: Radical resection of maxilla and exenteration of orbit for tumor primary in the maxillary sinus of a 70-year-old colored man. Death from meningeal infection. *Left,* anterior surface of specimen with eyeball at left. *Right,* posterior surface with optic nerve at left and portion of tumor in center. (H. Gordon, Louisville, Ky.)



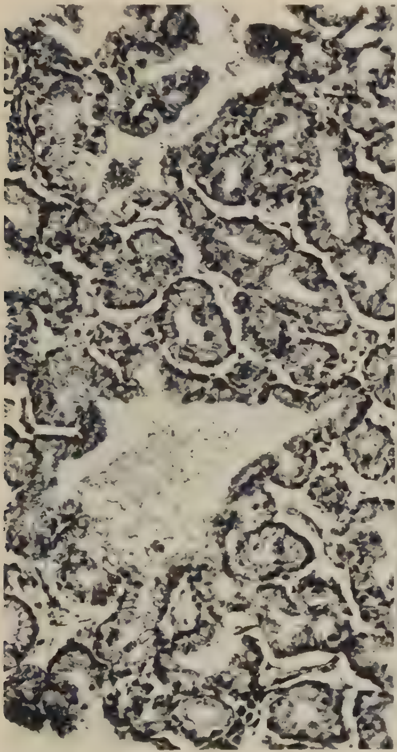
Histologic features. *Left,* squamous cell carinoma was diagnosed in sections routinely stained. *Right,* mucicarminophilic material (dark spots), demonstrated in tumor adjacent to relatively intact sinus epithelium, was present in other areas including solid central portions. Mucicarmine stain. x 62.



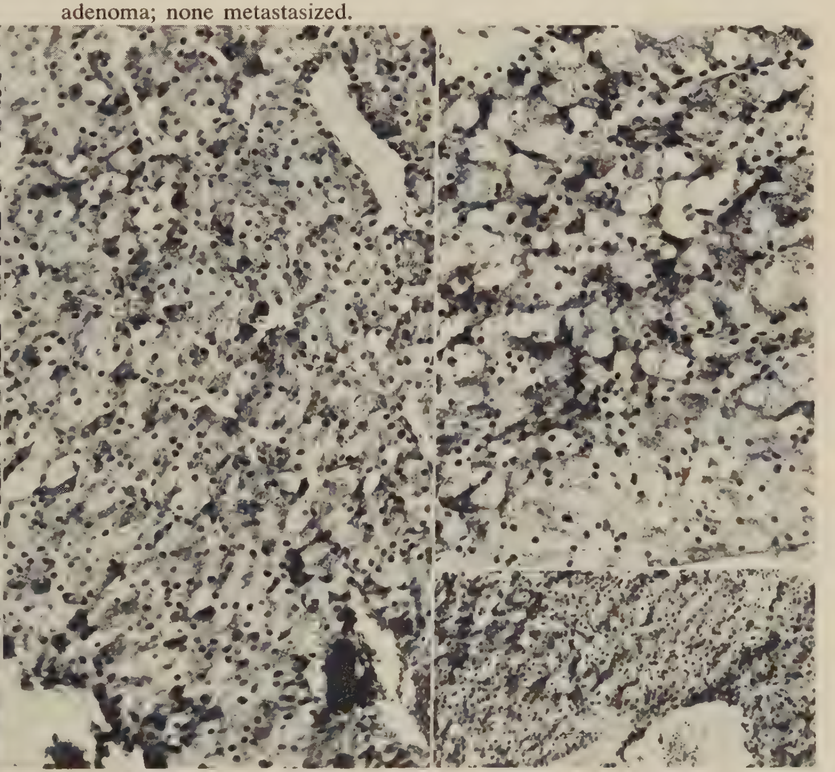
Mucicarminophilic cells, brilliantly stained, in foci deep within the tumor. Mucicarmine stains, x 185 and x 660.



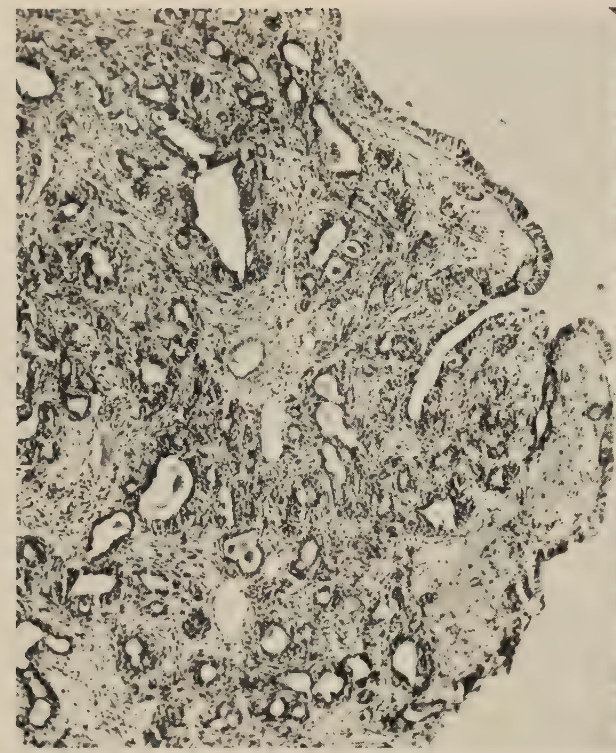
Polypoid adenomatous tumor, nasal cavity of a 73 year old man, with local extension and erosion of bone but no metastasis. Origin from terminal (intercalated) duct or acinar elements suggested by pattern and uniform appearance of cells lining both large and small glandular spaces. Practically no stroma. Only portions of contained secretion were palely mucicarminophilic. x 10, x 48. Occasional similar cases have been reported both as adenocarcinoma and adenoma; none metastasized.



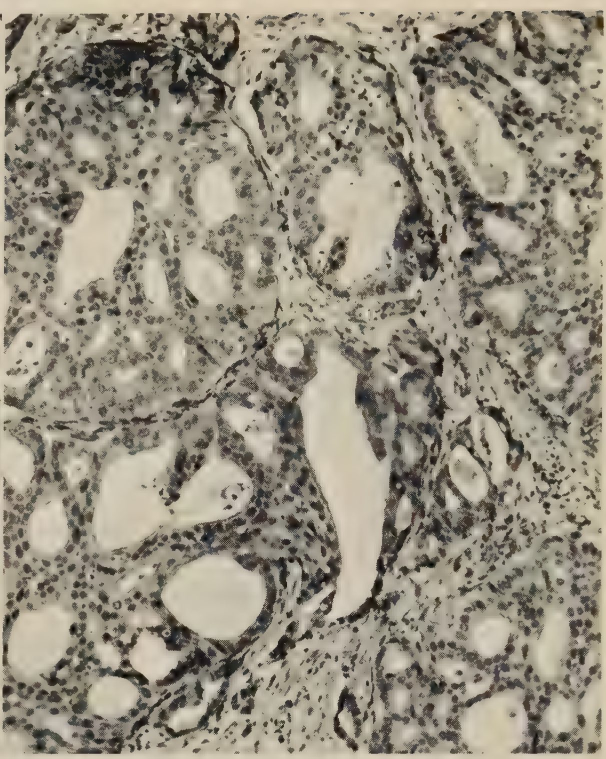
Detail of tumor above. Uniform, irregularly cuboidal cells with usually basal nuclei. x 145.



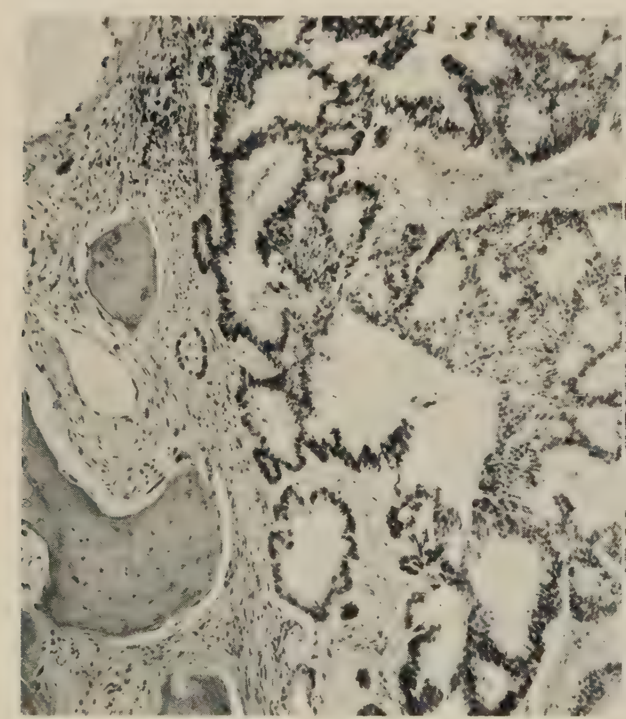
"Acinic-cell adenocarcinoma," of minor salivary glands of oral mucosa, analogous to those reported and described by Foote in the parotid gland. Six years after the first operation, the **fourth recurrence** (left x 160) was biopsied at same time as resection was performed of solitary, 1.5 cm., **lung metastasis** (right x 160, x 75). They are histologically identical. Moderate to marked granularity of cytoplasm resembles zymogen granulation of serous acinar cells. No mitoses.



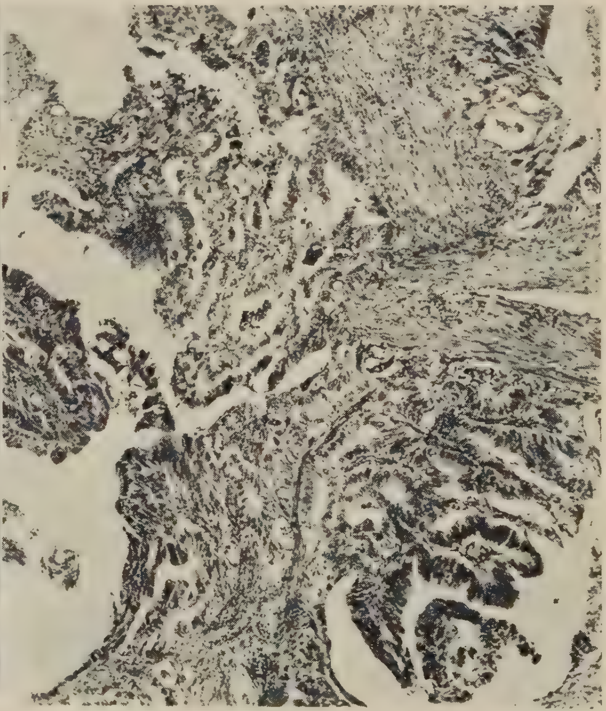
Mucosal adenocarcinoma, maxillary sinus. Surface respiratory epithelium largely preserved; tumor acini relatively well differentiated areas suggestive of origin in benign mixed tumor. x 75.



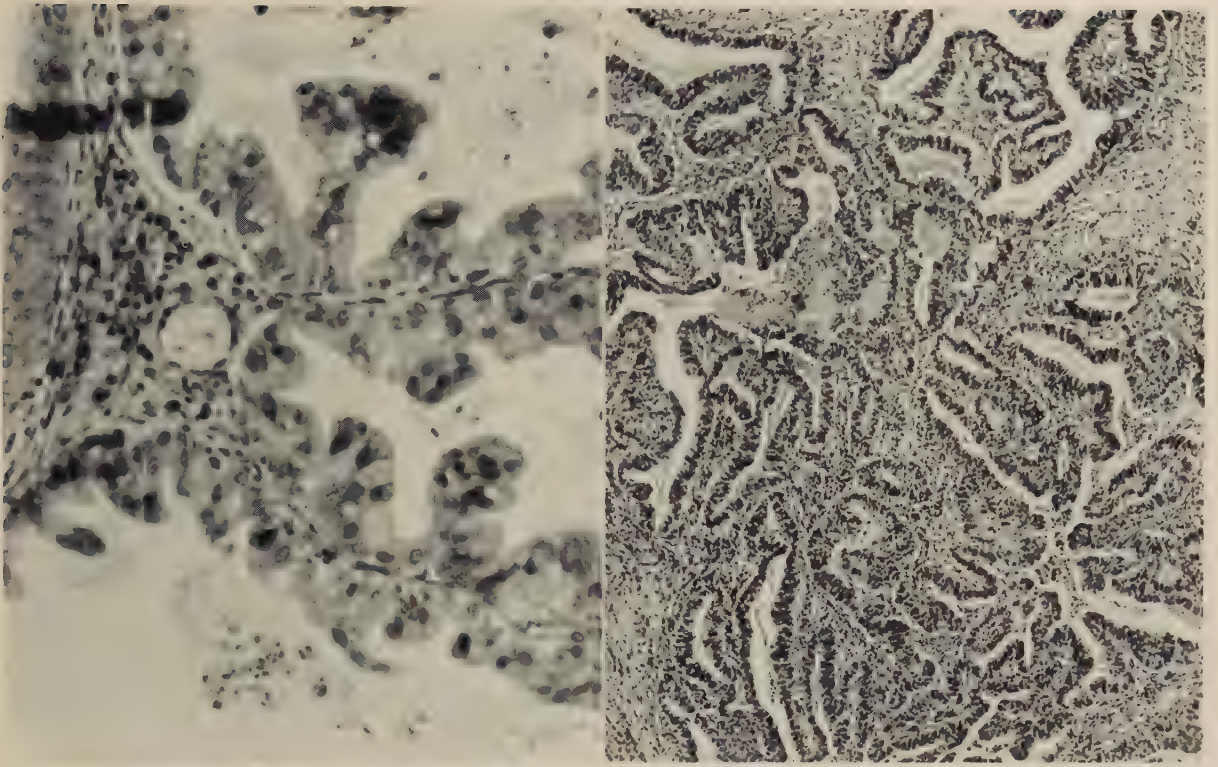
Adenocarcinoma, nasal mucosa; well differentiated. x 125.



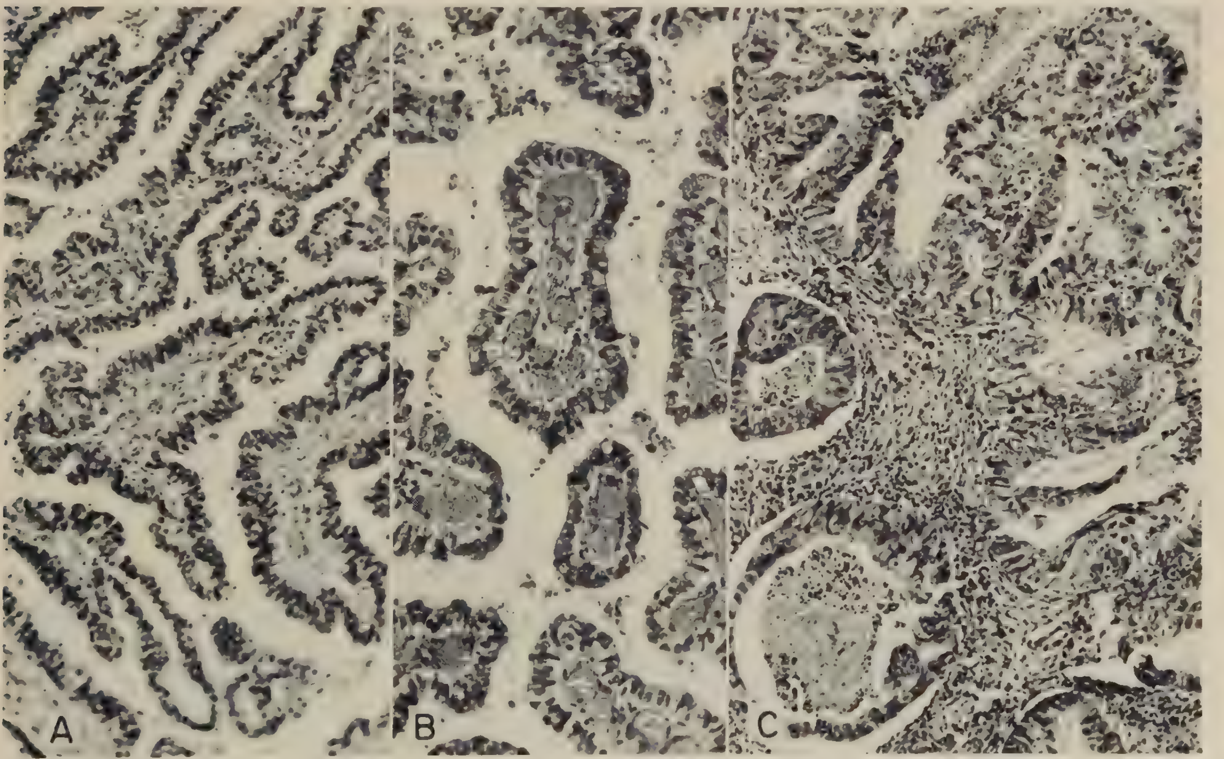
Adenocarcinoma, maxillary sinus, manifested clinically by increasing nasal obstruction for 6 months. Recurred in a more active form 2½ years after radical removal followed by 1800 mg. hours of radium. Mucus-producing tumor causing destruction of bone.



Adenocarcinoma, frontal sinus, in a 34 year old man with symptoms of "frontal sinusitis" for several years. Cellular tumor, with papillary projections into larger acini. x 76.



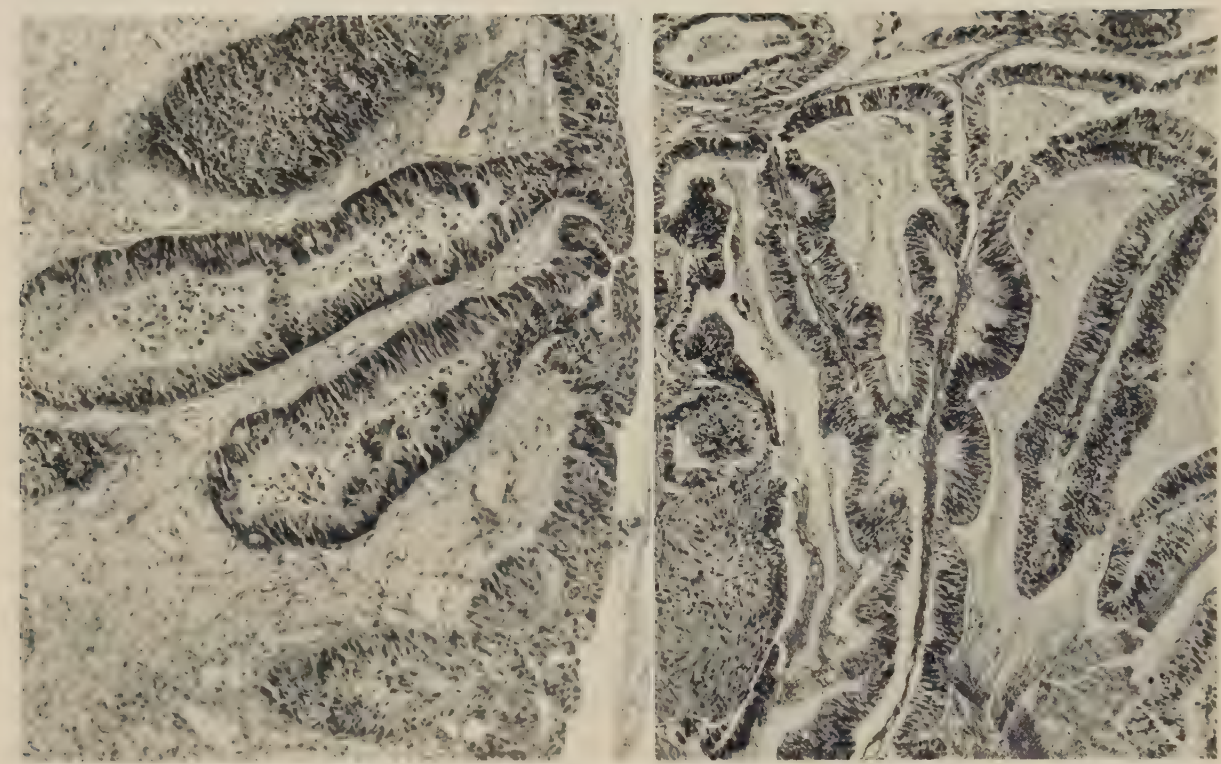
Papillary adenocarcinoma of the upper respiratory tract may be similar to or indistinguishable from similar neoplasms of the gastrointestinal tract. *Left,* primary carcinoma of ethmoid, in a 71 year old man who died a few months after radical excision. x 200. (S. Warren, Boston.) *Right,* papillary carcinoma involving nasal septum, inferior turbinate and nasopharyngeal wall of a 56-year-old man. x 62. Multiple recurrences excised during 3 year period.



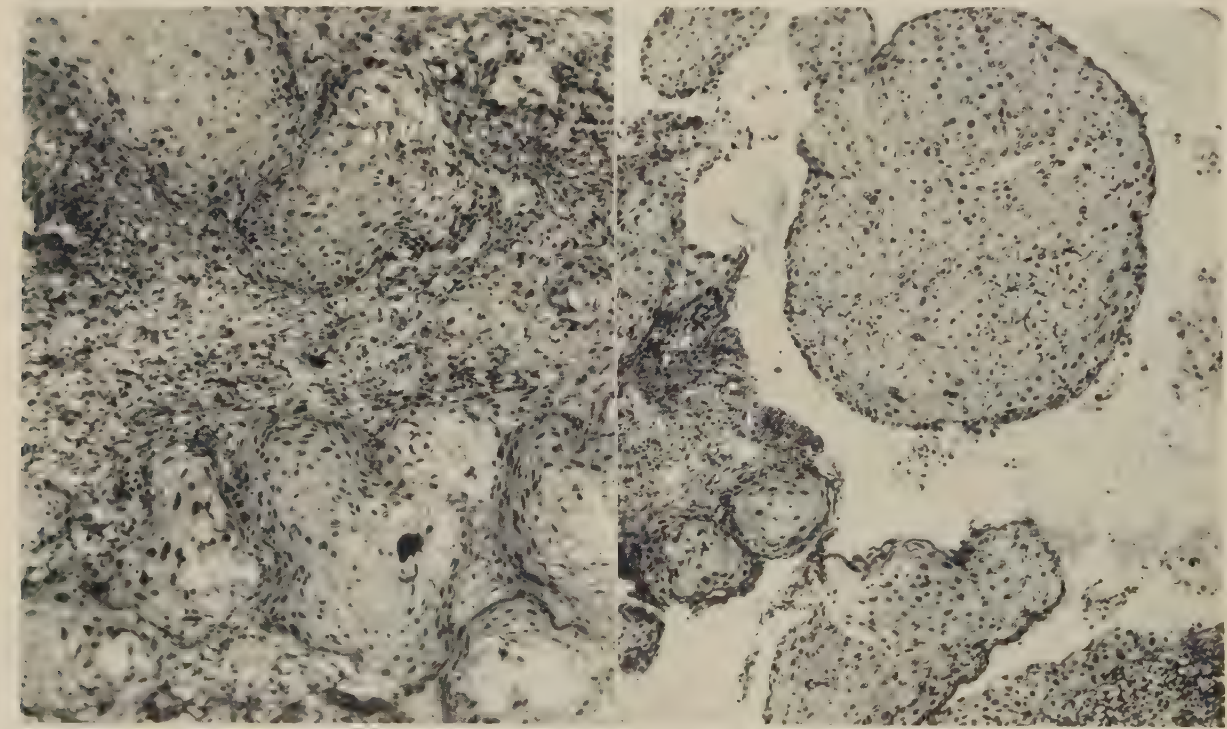
Histologic details, of tumor at right, above. **A** and **B.** Delicate papillary processes composed of columnar, usually non-ciliated cells, some with clear cytoplasm and central nucleus, surrounding delicate fibrovascular cores. x 125, x 160. **C.** More pleomorphic cellular pattern and stromal invasion. x 100.

ADENOCARCINOMA

("CYLINDRICAL CELL")

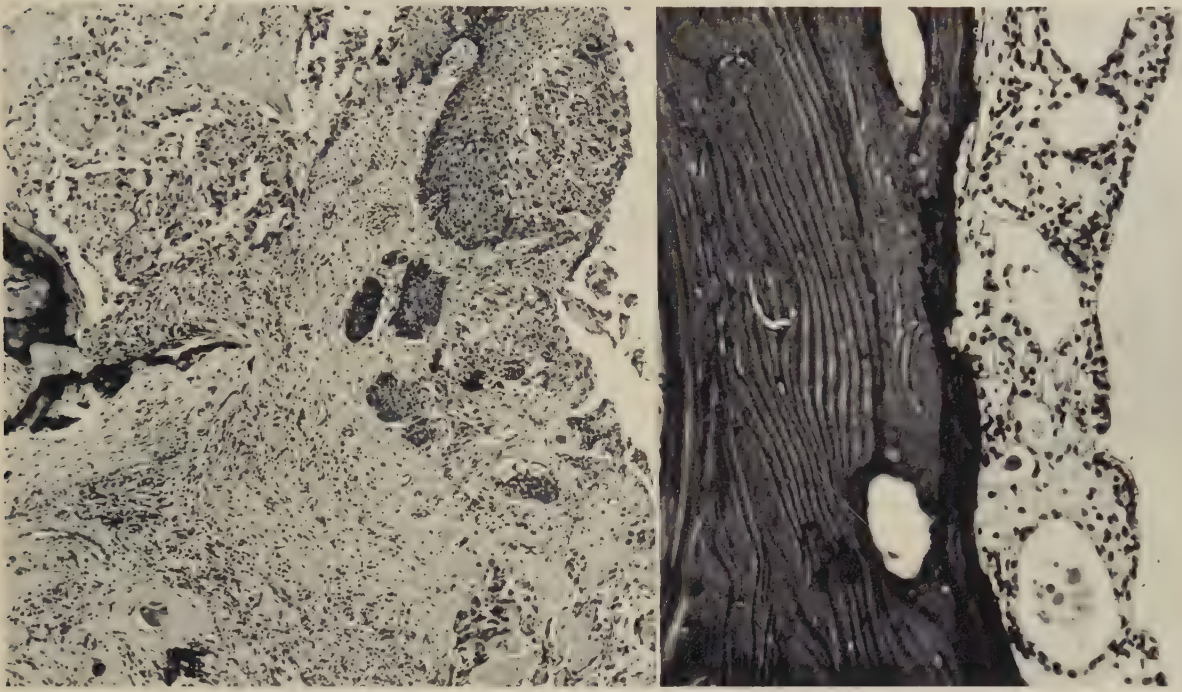


"Cylindrical cell" adenocarcinoma which appears to be arising from epithelium and ducts of ethmoid sinus. Tall columnar cells with multilayered nuclei. x 83, x 91. History of the 36 year old male patient revealed that a "nasal polyp" had been removed 4 years previously, following repeated epistaxis; 2 months later a small tumor (called benign) was removed from fronto-ethmoidal area; no symptoms until mucosanguineous discharge appeared 3 years later. Radical ethmoidectomy and x-ray therapy after biopsy diagnosis of adenocarcinoma. Extensive local invasion but no metastasis.

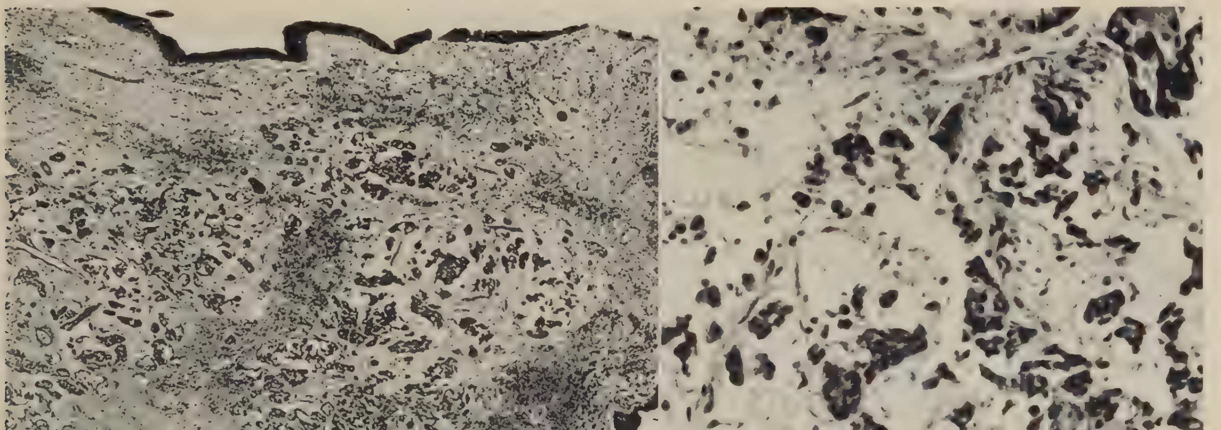


Squamous metaplasia, keratinizing at left, was pronounced in superficial and deep portions of the tumor. x 125, x 90.

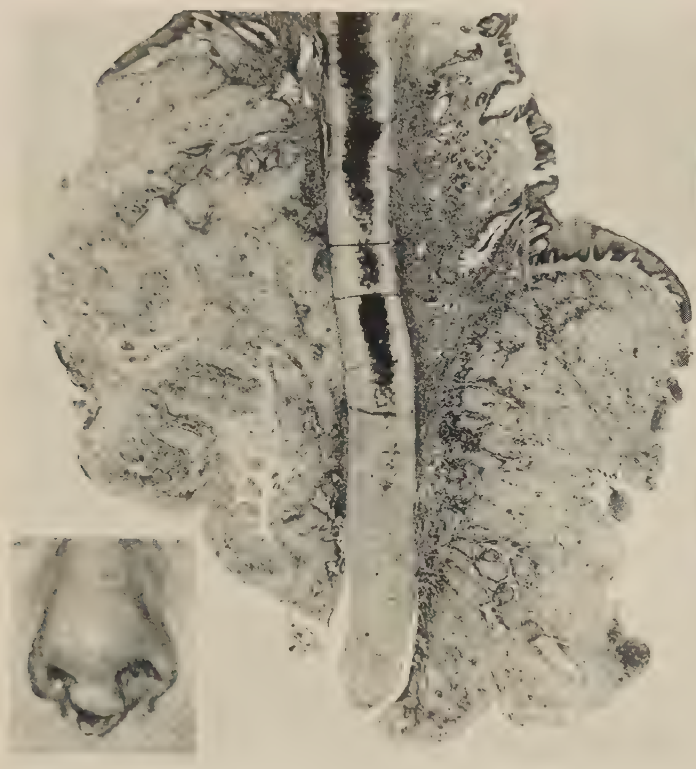
ADENOCARCINOMA WITH EPIDERMOID FEATURES
MUCINOUS ADENOCARCINOMA



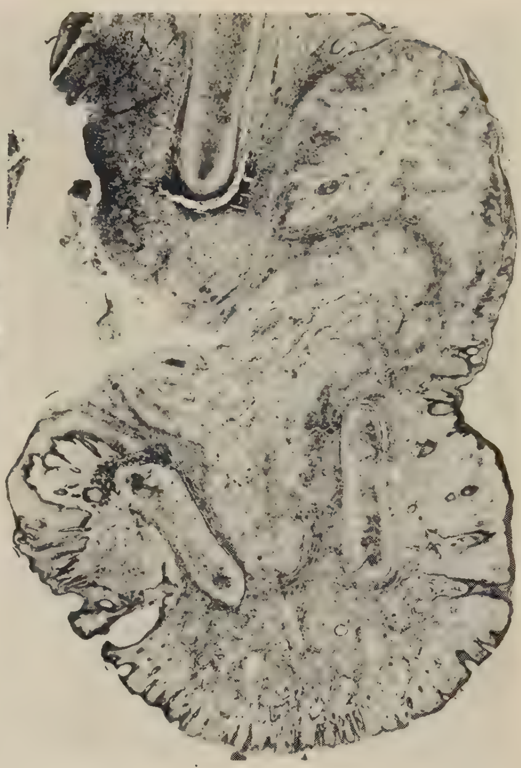
Adenocarcinoma and epidermoid carcinoma, intermingled in these fields, were found separately in other areas. Mass filled antrum and extended to ethmoids and nasal cavity of a 50 year old woman. This tumor could be adenocarcinoma with metaplasia to squamous type; mucoepidermoid carcinoma; or mixed adenocarcinoma and squamous carcinoma. x 62. Some portions of clear-cell area at right were mucicarminophilic. x 125. (V. M. Johnson, West Palm Beach, Fla.)



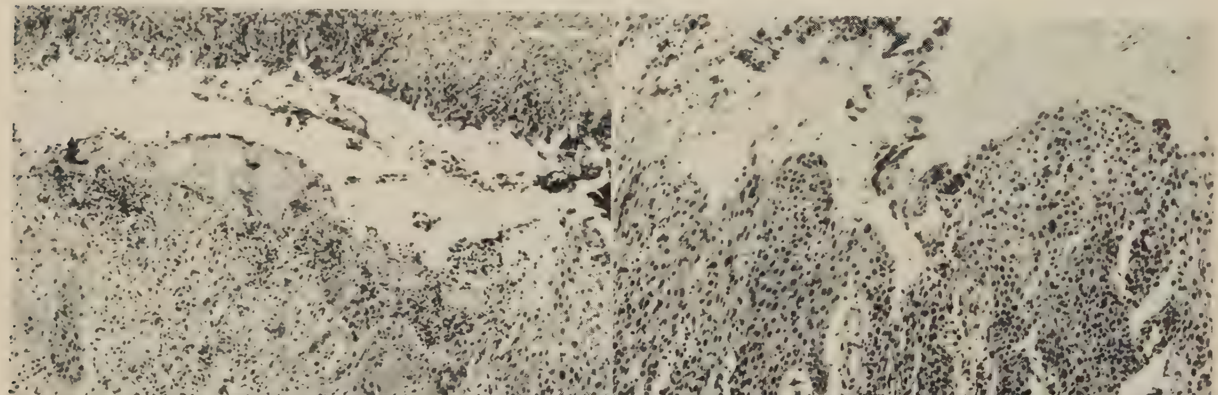
Mucinous (colloid; gelatinous) adenocarcinoma, which involved left frontal, ethmoid and maxillary sinuses, invading the orbit. Individual cells and irregular nests of cells, some retaining an adenoid structure in pools of strongly mucicarminophilic material. x 33, x 185.



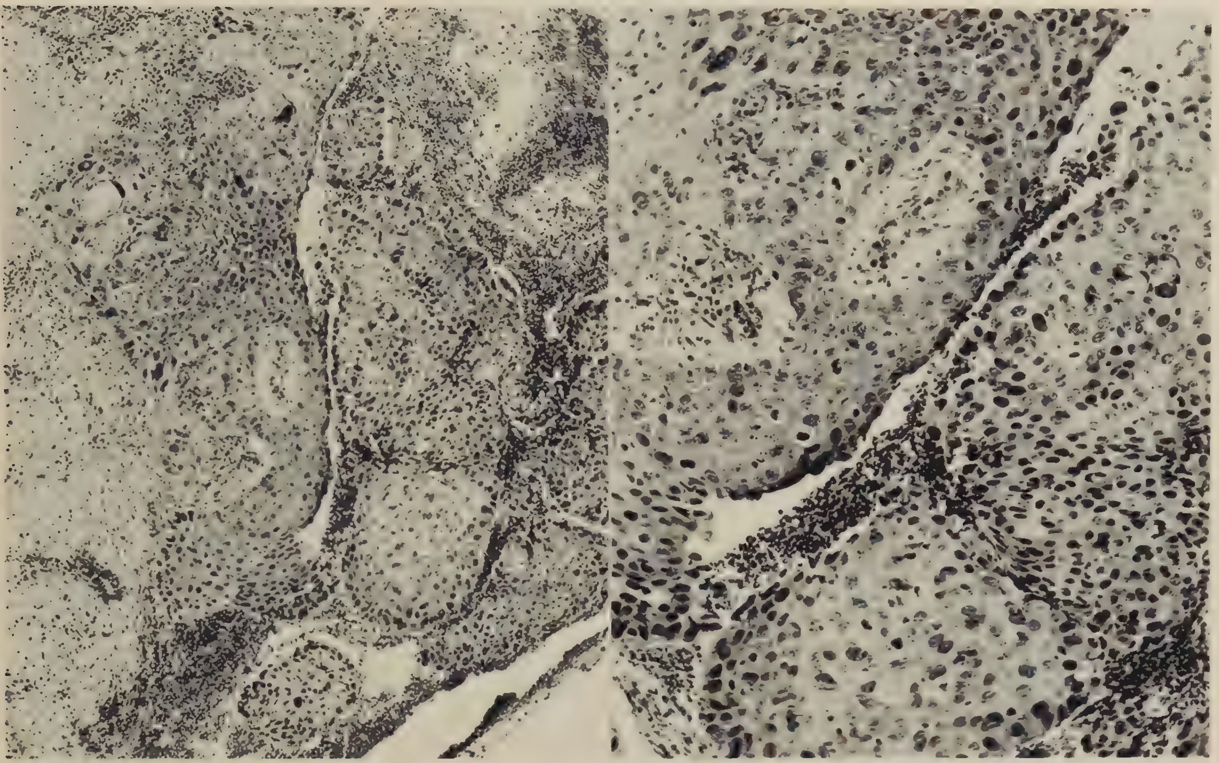
Squamous cell carcinoma, well differentiated, of nasal septum. Inset: Expansion of columella and erosion of the epidermis by tumor. Longitudinal section through excised mass shows tumor on both sides of cartilaginous septum; edge of perforation at bottom. x 10.



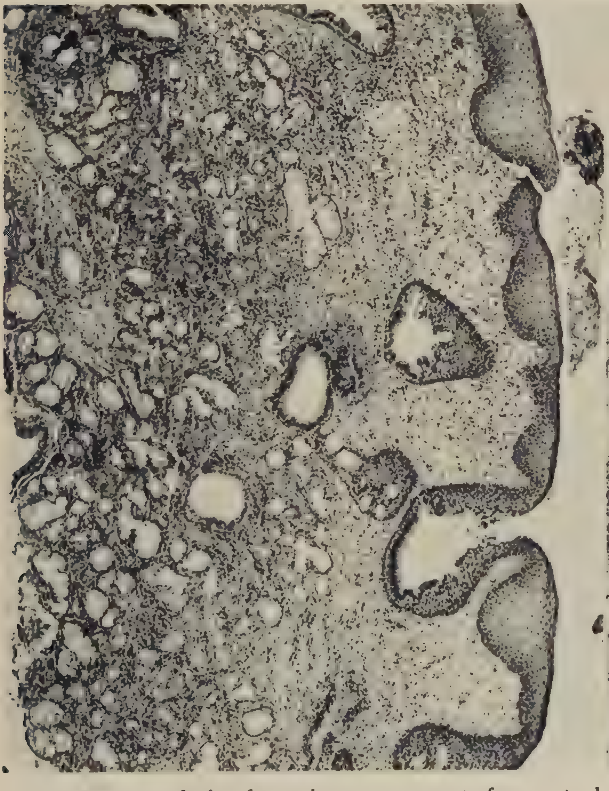
Septal perforation due to carcinoma of anterior nasal septum in another case. Well differentiated epidermoid carcinoma within the large septal defect and invading mucosa of the vestibule. x 7.



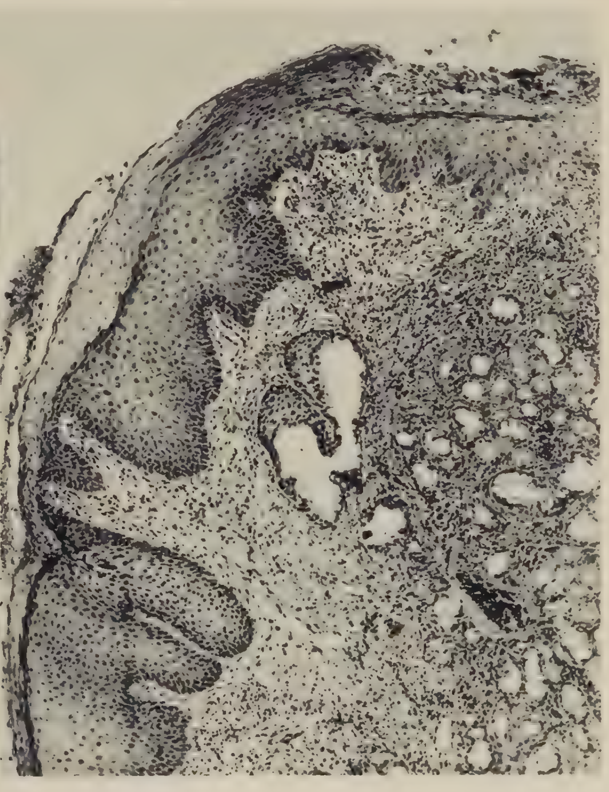
Non-keratinizing ("mucous membrane"; so-called transitional cell) carcinoma, causing extensive ulceration and perforation of nasal septum. Some attempt at squamous differentiation is seen in several strands. Sections from edge of ulceration. x 75, x 62.



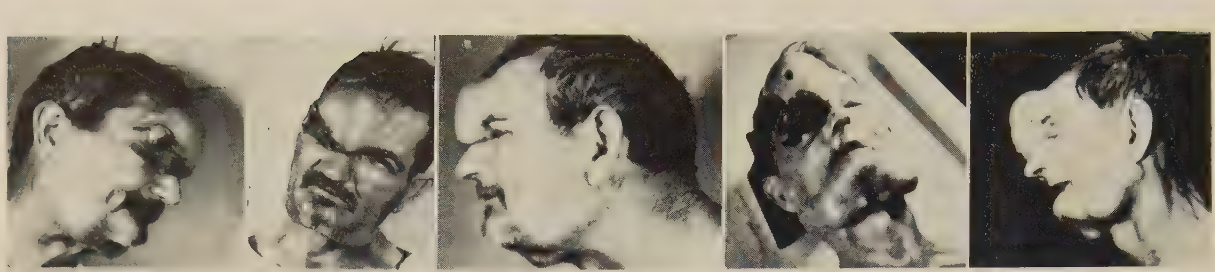
Epidermoid carcinoma, nasal septum, in 65 year old man with septal perforation of one year's duration. Fairly well differentiated tumor invading mucosa about the massive perforation. x 75. Bizarre cells, atypical mitoses, no keratin. x 160. (Suburban Hospital, Bethesda, Md.)



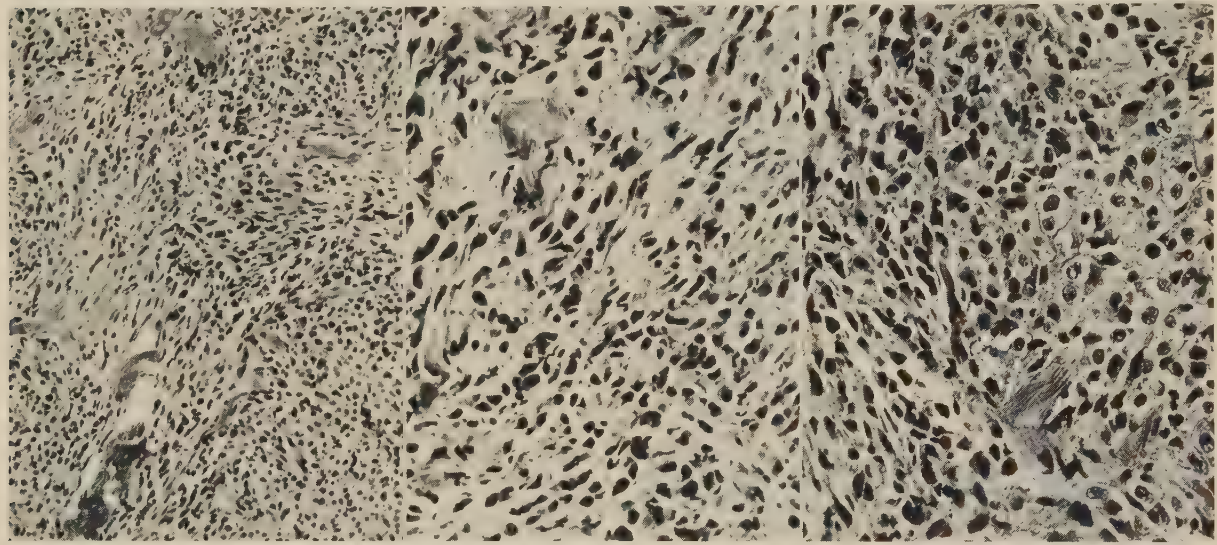
Squamous metaplasia of septal mucosa, remote from actual tumor which also involves duct epithelium. x 48.



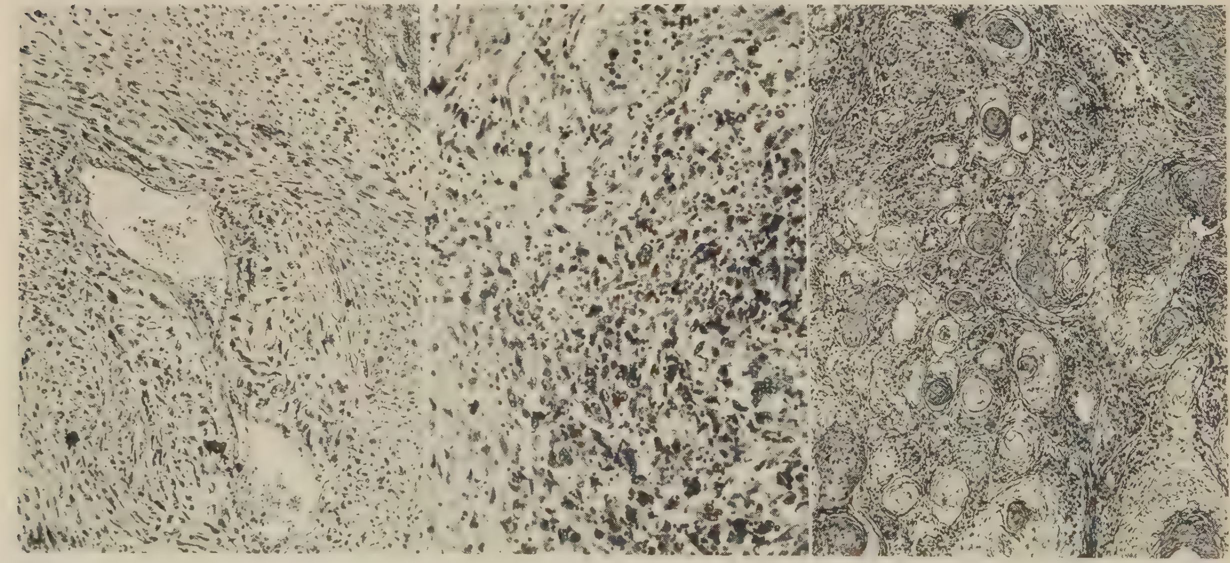
Acanthosis and parakeratosis merging into **leukoplakic dyskeratosis** (at top). Mucosa in field adjacent to infiltrating carcinoma. x 75.



Tumor, primary in right frontal sinus. Frontal headache was initial symptom. It extended into right orbit, all other paransal sinuses except left maxillary, and posteriorly into the right anterior cranial fossa. Metastases only to submandibular nodes and to one adrenal. Three clinical pictures on left taken 2 months before death; two on right, post mortem. Note downward and lateral displacement of eye, a typical feature of frontal sinus tumor, and bilateral submandibular metastases. (H. Derman, Kingston, N. Y.)



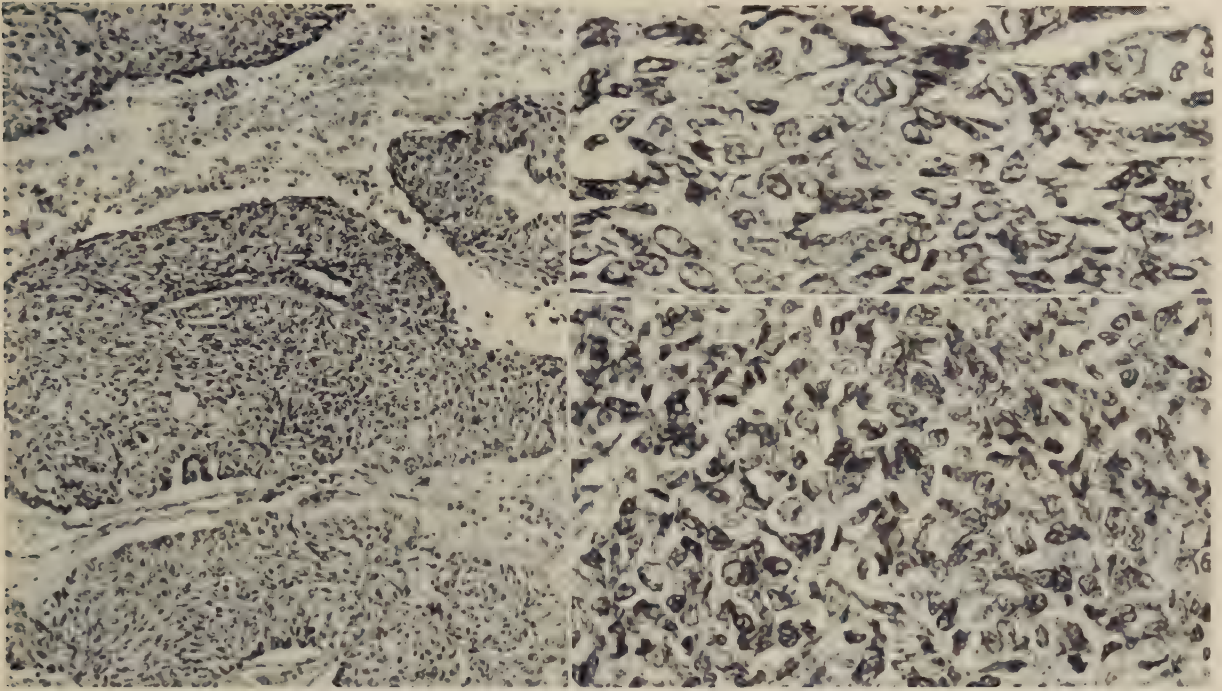
Three fields from original biopsy specimen, diagnosed meningeal sarcoma by several pathologists. *Left* and *center,* sarcomatoid areas. x 100, x 235. *Right,* field suggestive of poorly differentiated carcinoma. x 260.



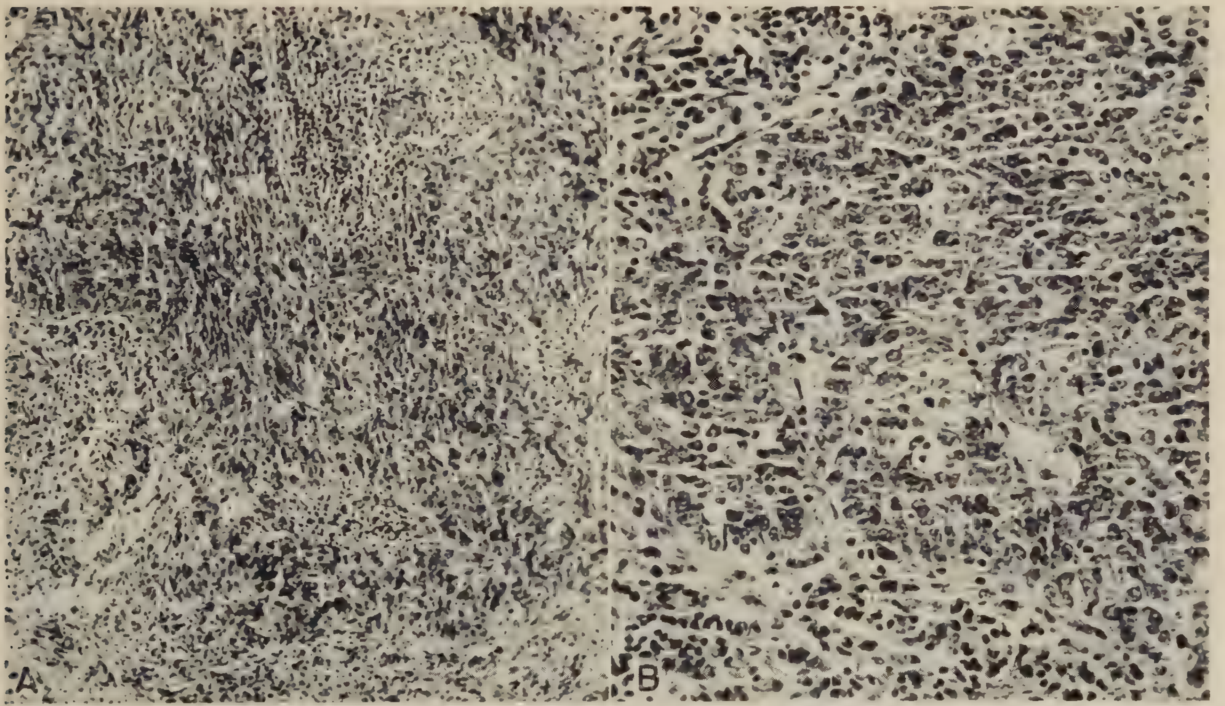
Spindle cell sarcoma-like features present (*left,* x 90) in 7 of 9 post mortem specimens from primary tumor. Occasional foci with plump cells, more epithelial in character, blended with slender spindle cells, (*center,* x 125). Areas of well-differentiated squamous cell carcinoma in only two specimens (*right,* x 48). No strongly mucicarminophilic material evident in any part of tumor examined.

POORLY DIFFERENTIATED EPIDERMOID CARCINOMA

VARIED TYPES TERMED "TRANSITIONAL CELL"



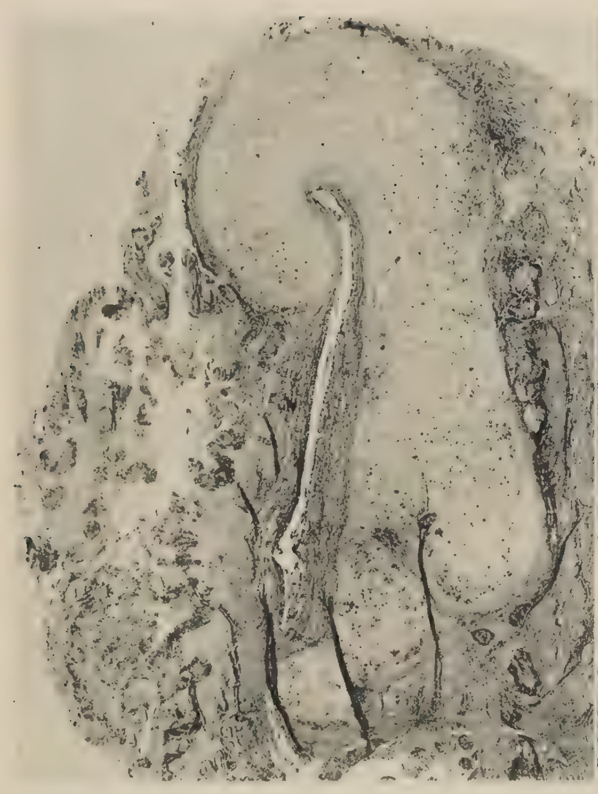
Carcinoma of pharynx, one of variants termed "transitional cell." Papillary, partly cylindric cell character of biopsy from the surface of a tumor, unquestionably carcinoma, from a 63 year old man. x 125. Fields from primary tumor *(upper)* and cervical lymph node metastasis *(lower)*, which showed no evidence of keratinization or squamous differentiation. Both x 440.



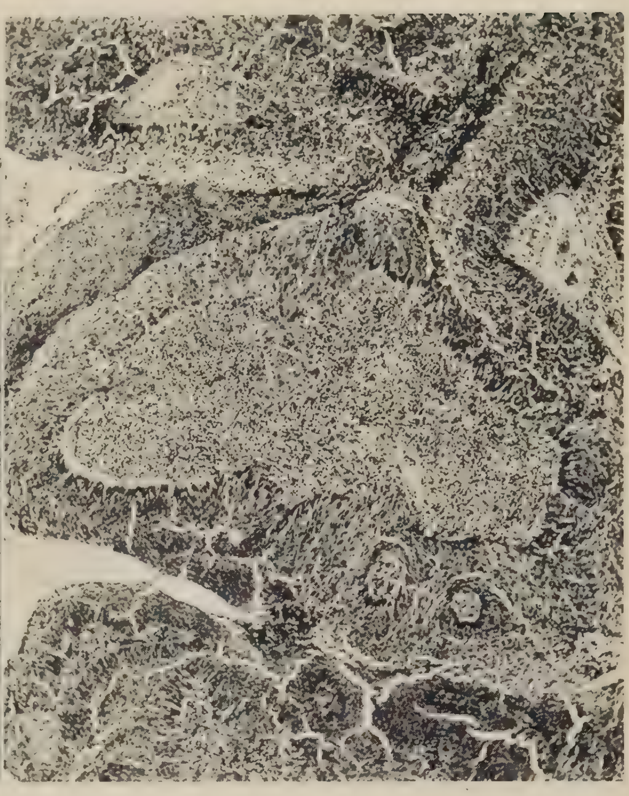
Metastatic "lymphoepithelial" carcinoma, cervical lymph node, in a young man whose first symptom was deafness. Like the primary nasopharyngeal tumor, the lymph node shows an abundant lymphocytic component in the ill-defined cords and strands (**A,** x 125) and suggestive alveolar structure (**B,** x 275) of the metastatic tumor. In some areas *(left)* the neoplastic tissue is rather sharply defined from adjacent normal lymphatic tissue of the node. However, histologic differentiation of such tumors from some forms of malignant lymphoma may be difficult, particularly in lymph nodes extensively involved.

NASOPHARYNGEAL CARCINOMA

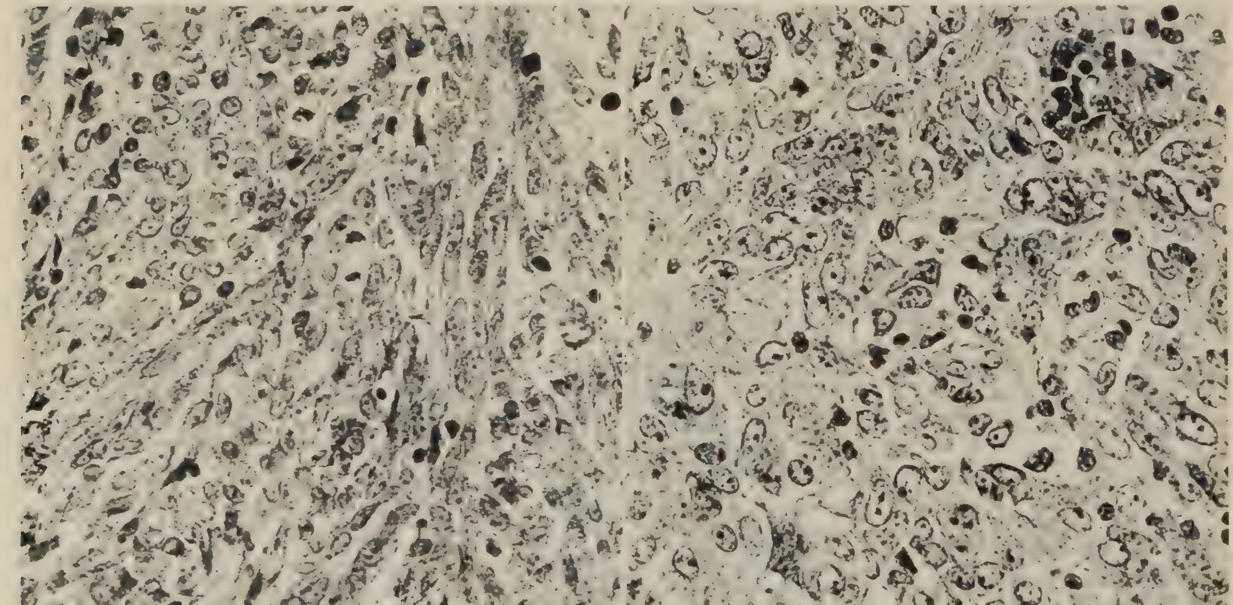
VARIED TYPES TERMED "TRANSITIONAL CELL"



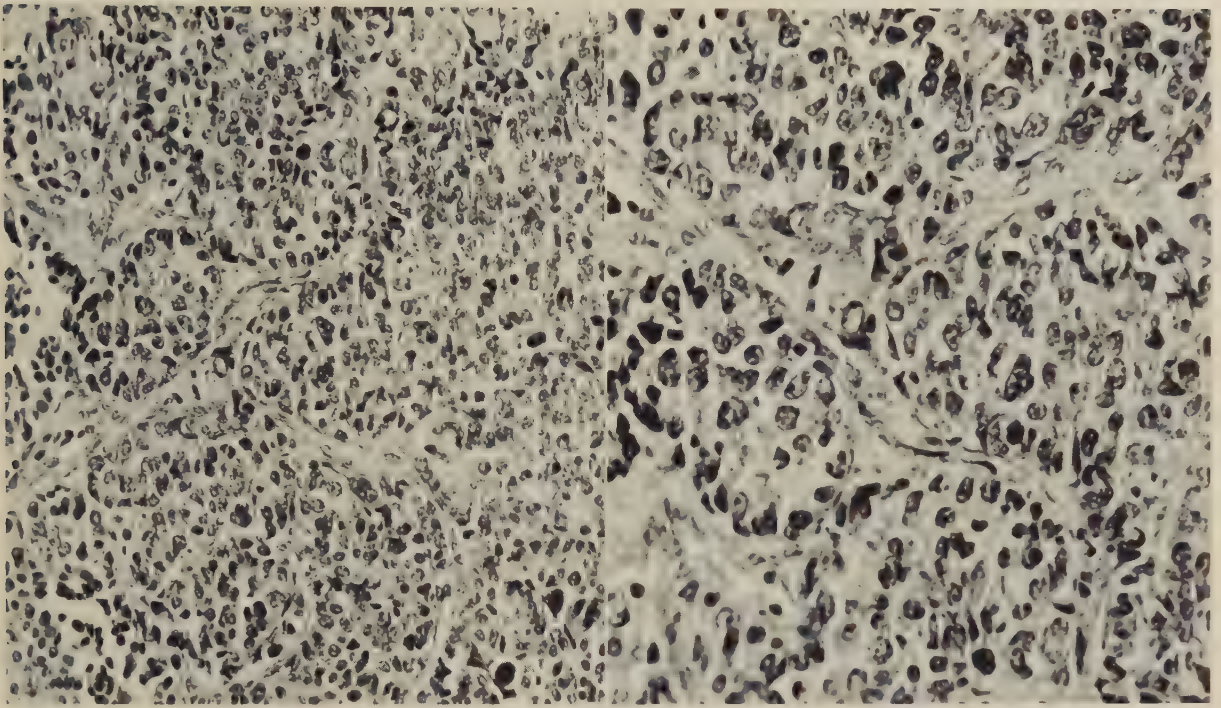
Poorly differentiated epidermoid carcinoma, primary in fossa of Rosenmüller, extensively invading region of eustachian tube. With such involvement deafness may be an initial symptom. x 13.



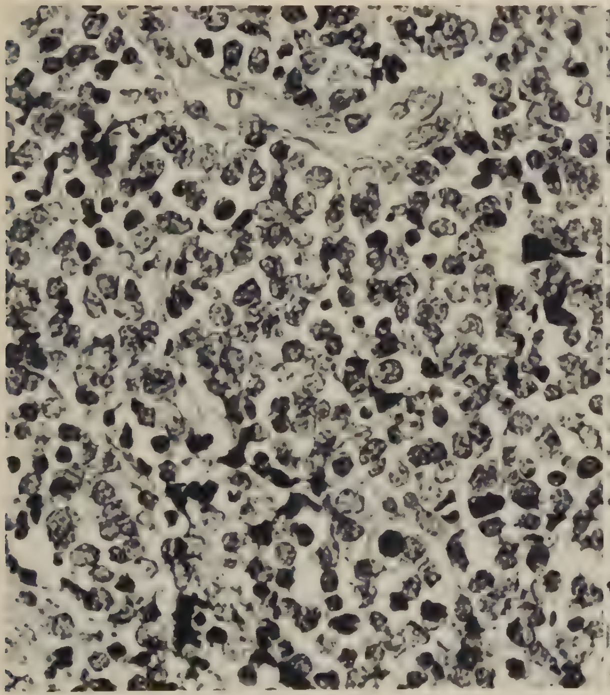
Papillary surface of carcinoma of nasal cavity which extended posteriorly to nasopharynx and eroded through left nasal bone in an 85 year old man. Composed of slender cylindrical cells. No keratinization. x 55.



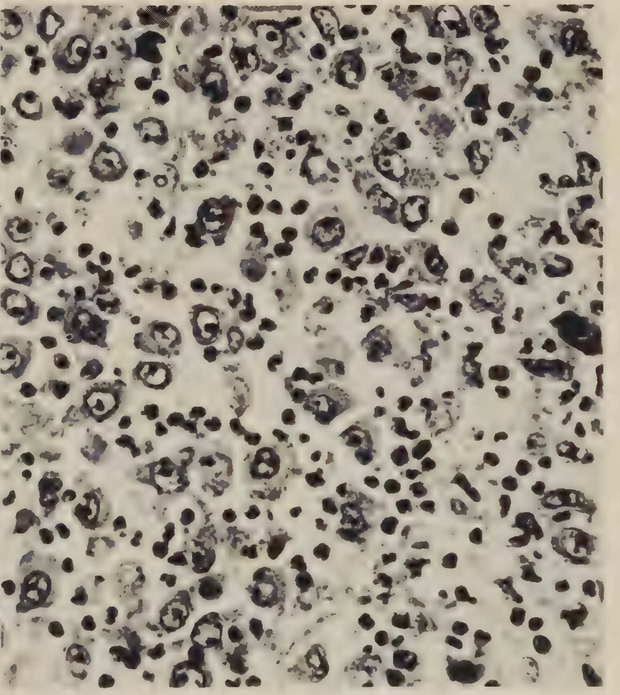
Metastatic undifferentiated tumor, cervical nodes, in a patient with primary tumor in the nasopharynx and neurologic symptoms. Considered probable undifferentiated carcinoma. Histologic cell type may be similar to forms of lymphosarcoma, reticulum cell sarcoma and the epithelial cell of so-called lymphoepithelial carcinoma. Both, x 600.



Undifferentiated malignant tumor, possibly anaplastic carcinoma, of tonsil in a 59 year old man. Alveolar pattern present throughout and sharp demarcation from adjacent tonsillar tissue, accentuated by reticulum stains, considered compatible with carcinoma. x 255, x 355. Similar problems and difficulties in interpretation of tumors of the upper respiratory tract are often encountered.

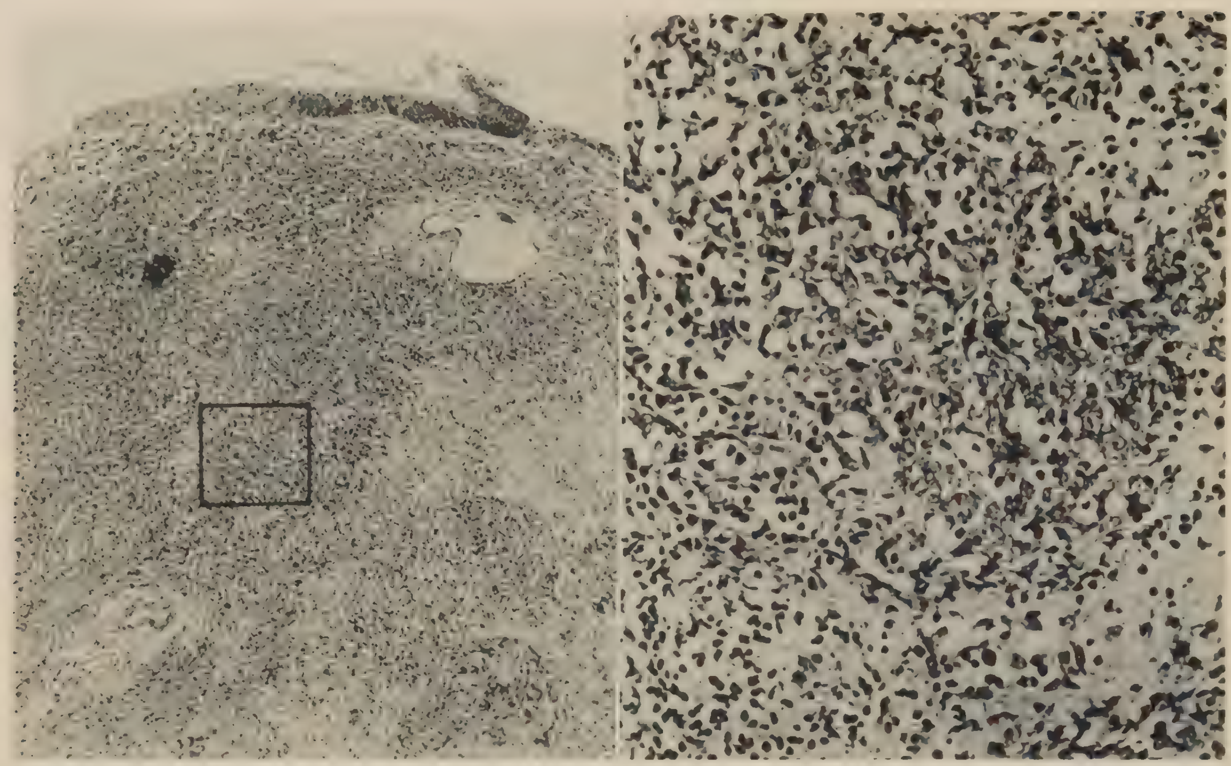


Malignant tumor, nasal cavity, in a white man 62 years of age, diagnosed variously as anaplastic carcinoma, malignant lymphoma, sympathicoblastoma and malignant melanoma. x 440.

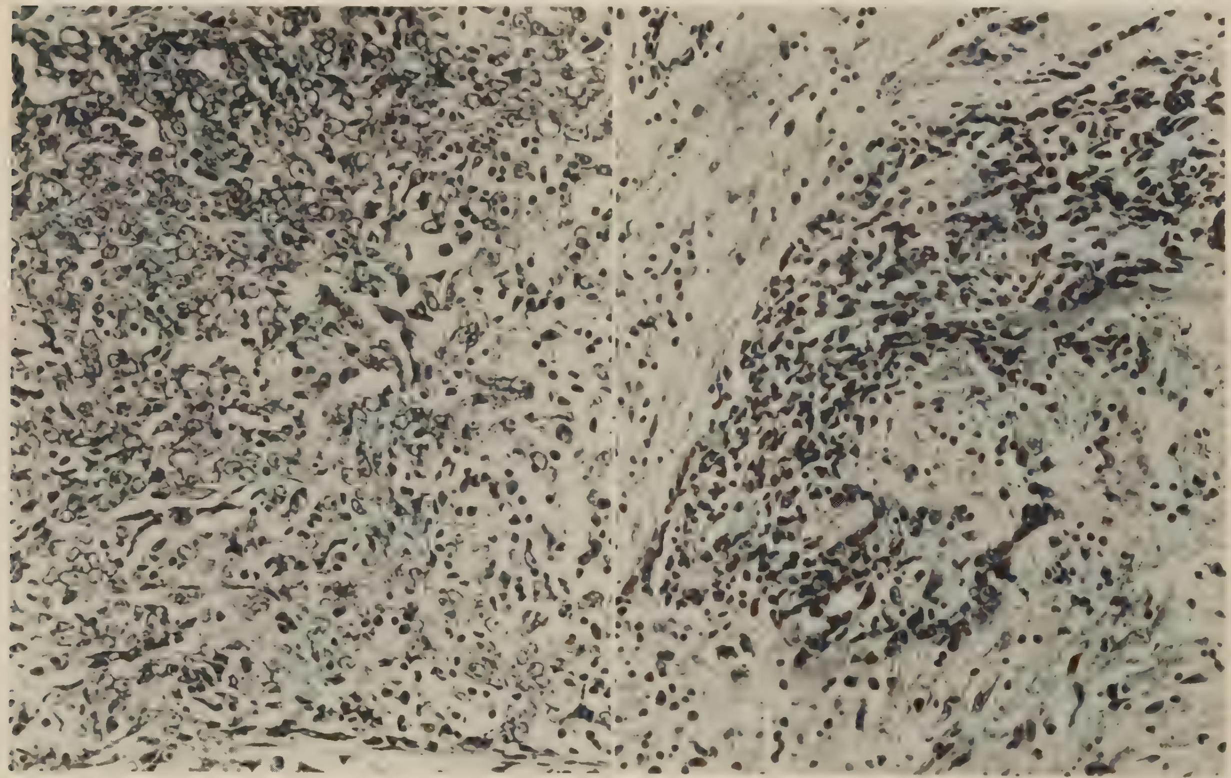


Pleomorphic malignant tumor, pharynx, in a 19 year old male. Dissociated neoplastic cells and inflammatory cells in this field. x 450. Diagnoses included malignant lymphoma, carcinoma, and malignant melanoma.

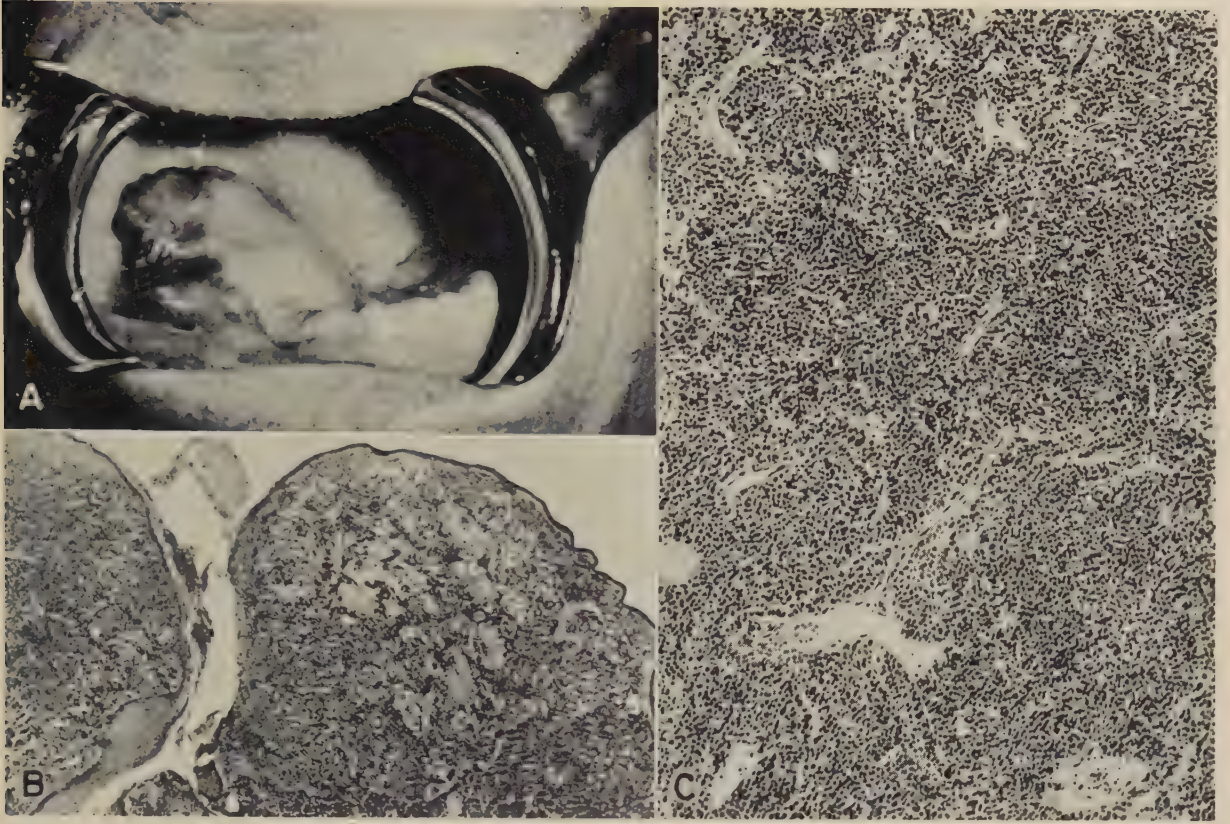
Final diagnosis in these undifferentiated tumors is at times indicated by clinical course and method of spread.



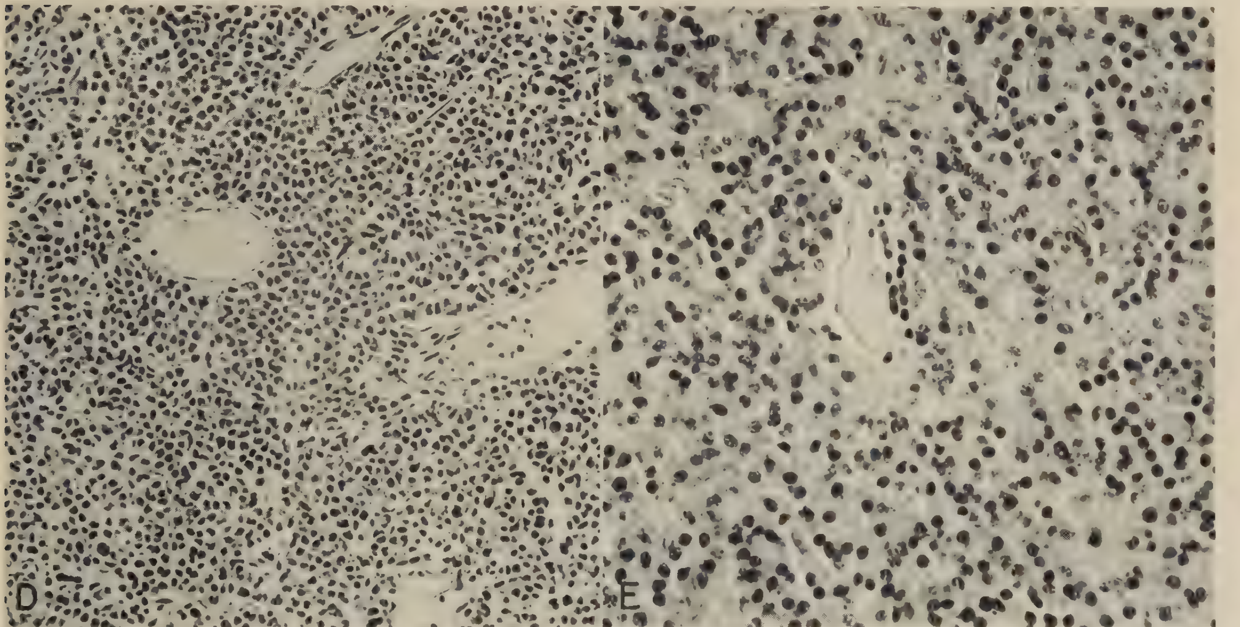
Primary malignant tumor of nasopharynx that extended through foramen lacerum to cranial cavity. **Classic neurologic syndrome** in 54 year old white man. Successive paralysis of VI, V, IV, III and VII cranial nerves. Nasopharyngeal biopsy shows focal ill-defined masses of tumor in portions of stroma. x 55. Detail of blocked area. x 260.



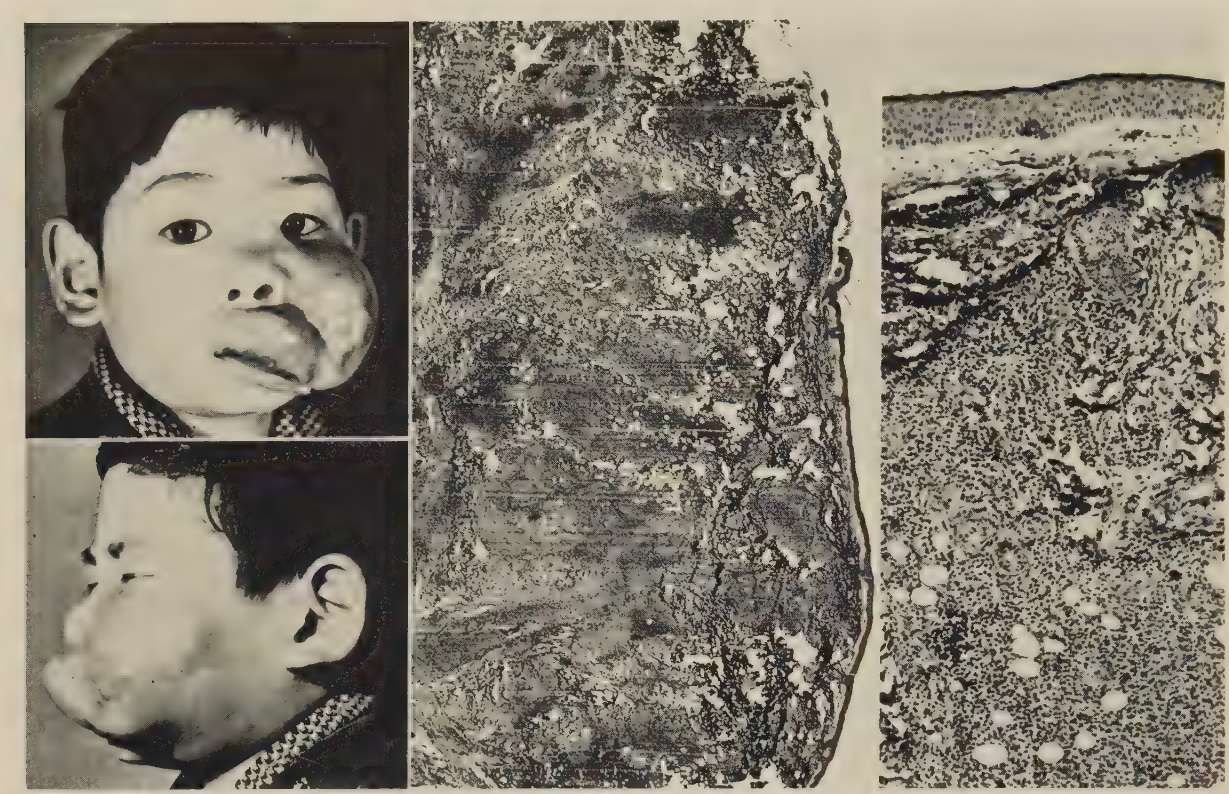
Cervical lymph node metastases of same case. No further differentiation evident in any areas. Probable malignant lymphoma of primitive cell type favored as diagnosis, rather than lymphoepithelial carcinoma, despite clinical behavior considered more characteristic of carcinoma. Both x 260.



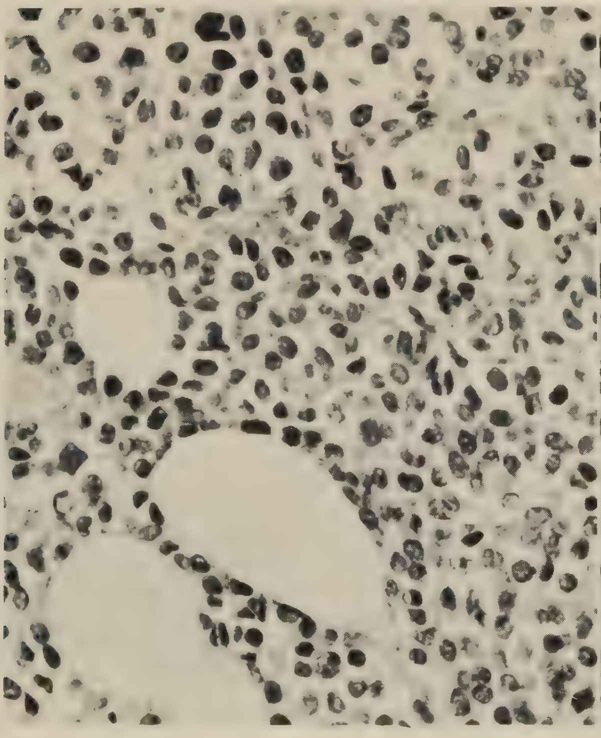
Extramedullary plasmacytoma. A. Smooth nonulcerated mass, clinically evident on hard palate of 64 year old man. Involvement of nasal cavity and sinuses on same side and multiple defects in skull. (Figi, Broders and Havens, Mayo Clinic: Ann. Otol., Rhin. & Laryng. 54:283, 1945.) **B.** Low power view of tumor on posterior tonsillar pillar of eight months' duration in a 72 year old man. (C.A. Larson, Fargo, N.D.) **C.** Plasmacytoma, primary in nasal cavity of a 78 year old man. Well vascularized tumor composed of sheets of cells of uniform type. x98.



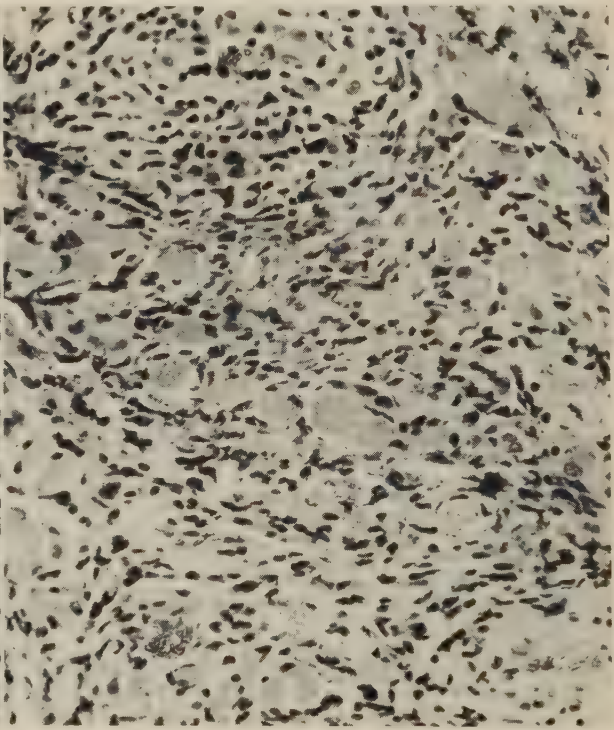
D. Higher power of **"C."** Loosely arranged and dissociated cells in a prominently vascularized stroma. x175. **E.** Section from another plasmacytoma that involved nasal cavity, antrum and pharynx of a 72 year old man. Very well differentiated tumor composed of uniform cells with plasma cell nuclei, numerous multinucleated forms, and very rare mitotic figure. x400. Beginning as "nasal polyp," it recurred one year after removal. (S.S. Hall, Clarksburg, W.Va.)



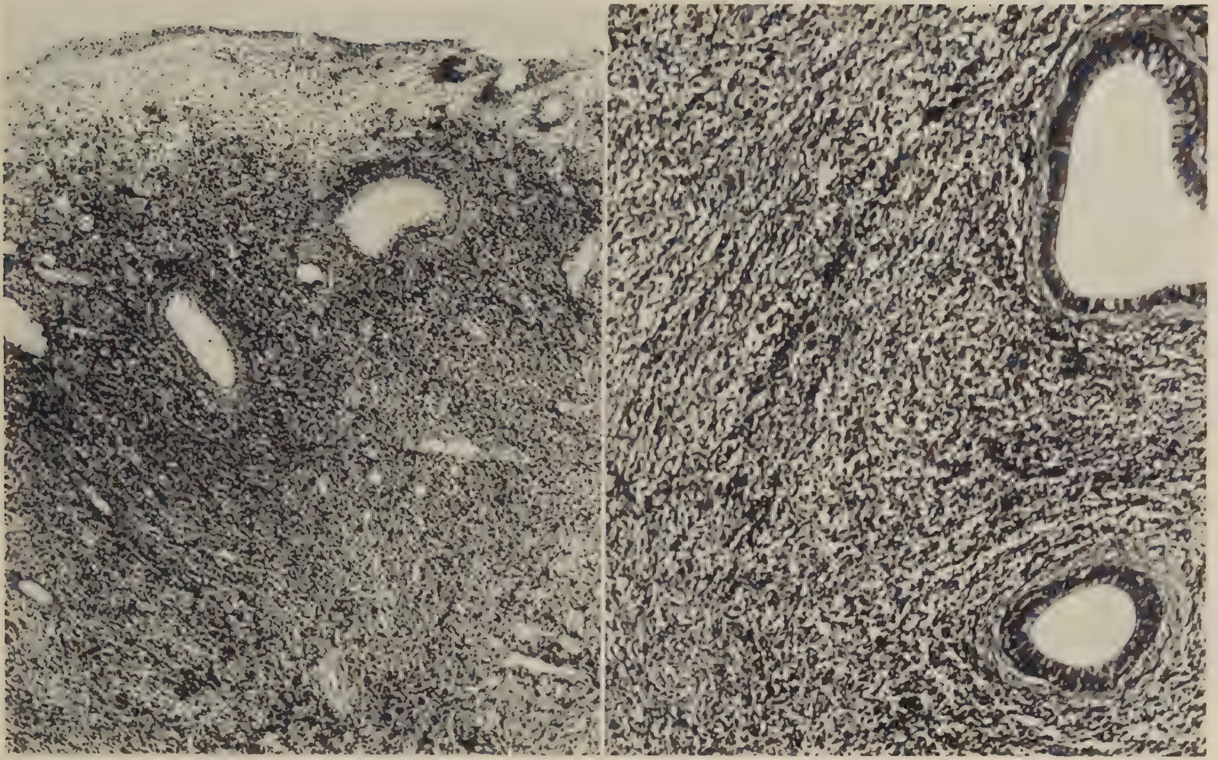
Malignant lymphoma (lymphosarcoma), of 1 year's duration, primary in region of maxillary sinus. X-ray therapy retarded growth, but only temporarily. Heavy cellular infiltration of subcutaneous tissue and skin. x 11. Architecture of the tissue is not destroyed. x 83.



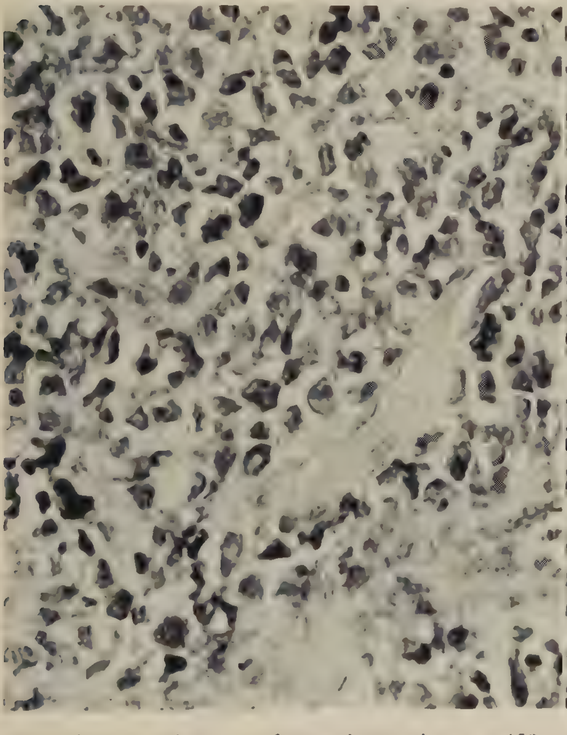
At higher magnification, the cells are undifferentiated, though evidently not epithelial; many nuclei are hyperchromatic; frequent mitoses. x 625.



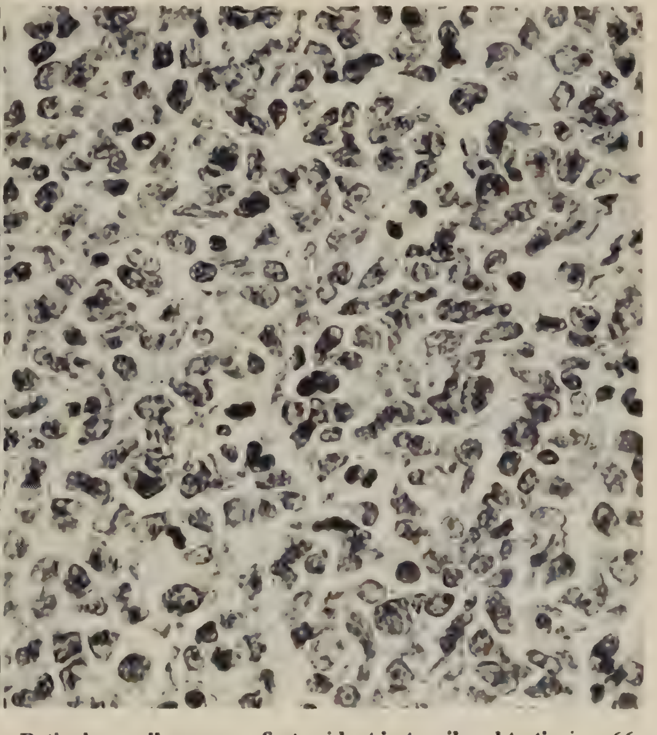
Lymphosarcoma, face, extending into nose. The muscle is infiltrated by undifferentiated cells with hyperchromatic nuclei. x 315.



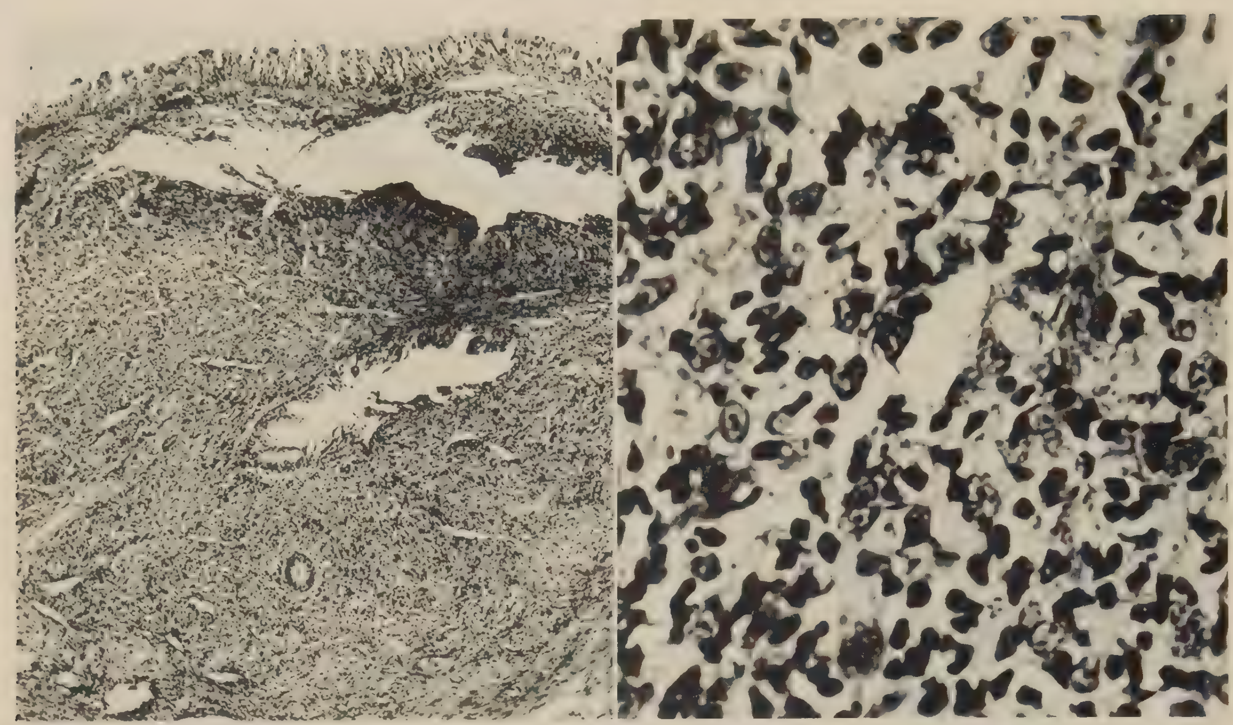
Reticulum cell sarcoma, initially manifest in nose and testis: *Left,* densely cellular infiltration of mucosa of middle meatus. x 62. *Right,* tubules of epididymis are widely separated by diffuse infiltration of malignant reticulum cells. x 100.



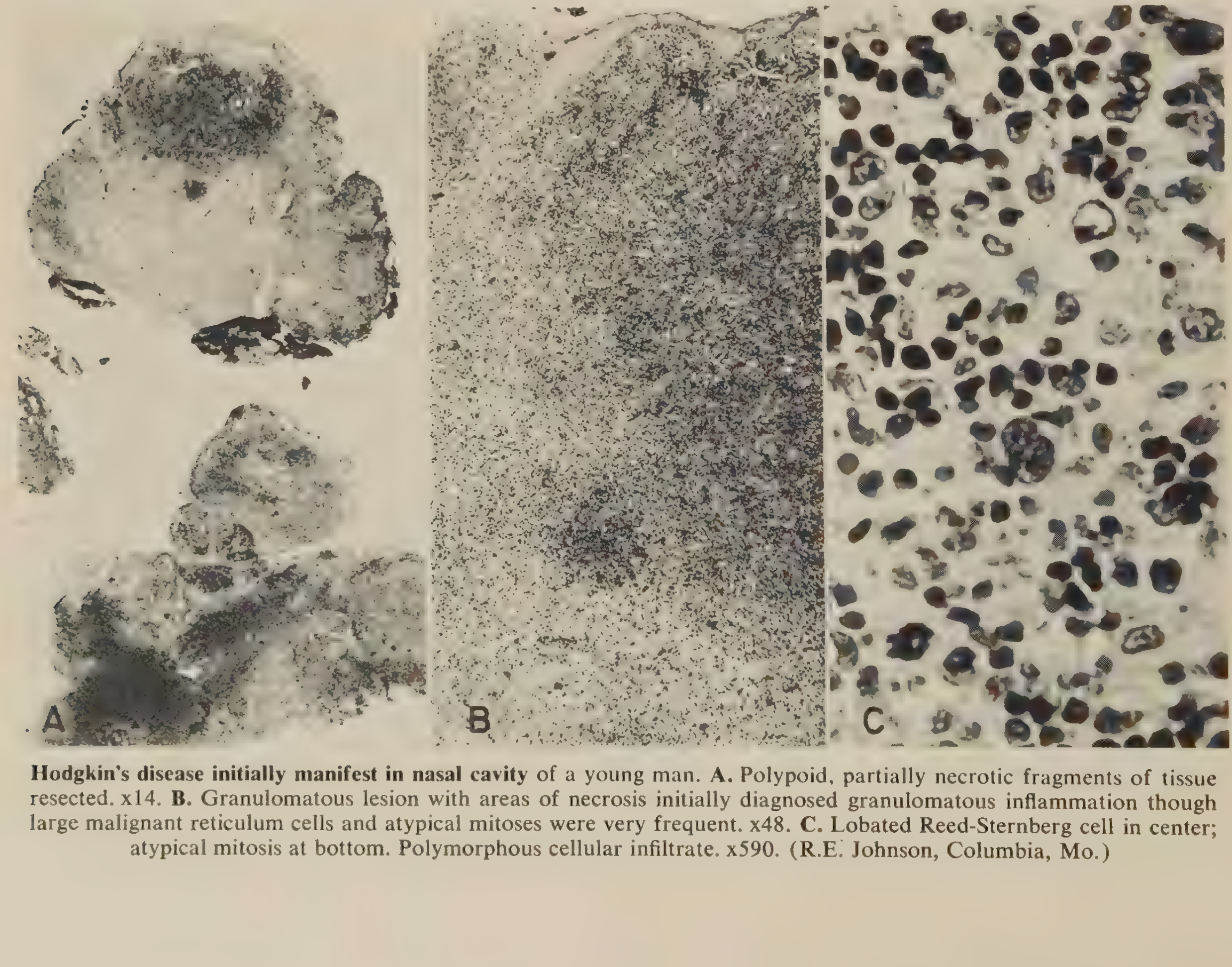
Field from nasal tumor of case shown above. x 450.



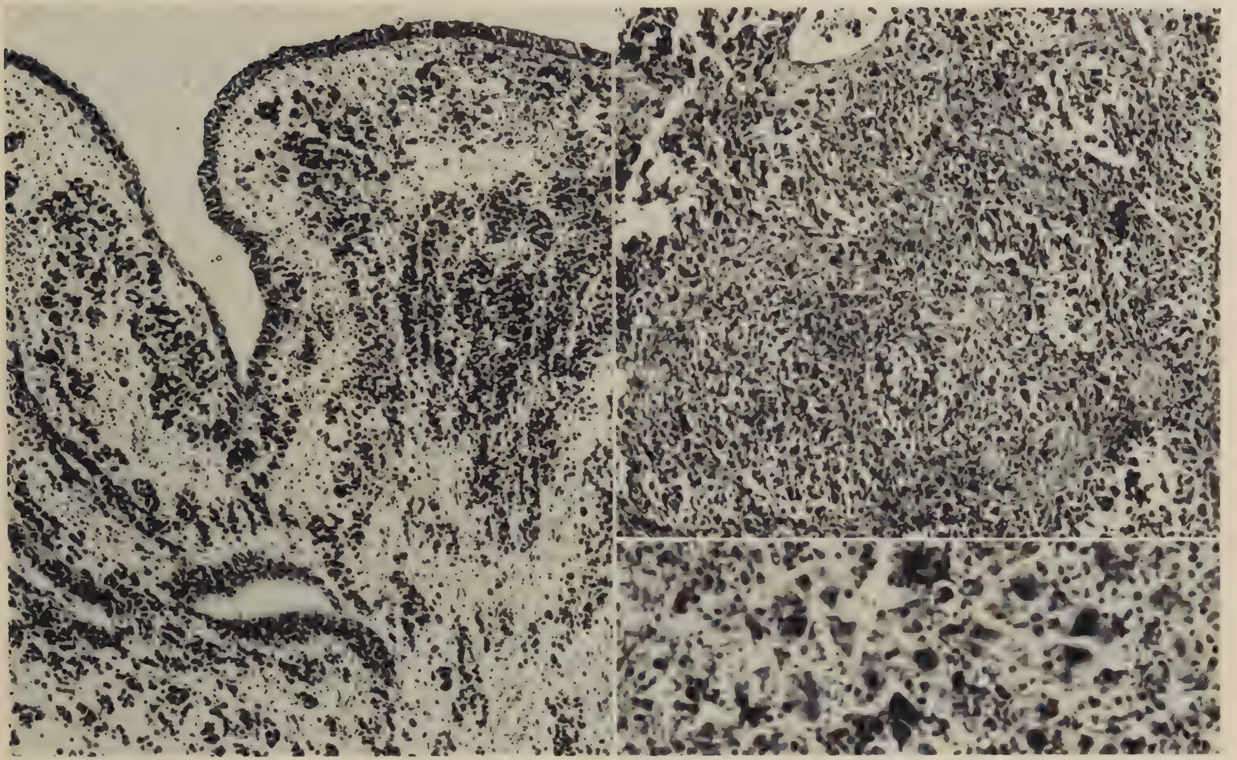
Reticulum cell sarcoma, first evident in tonsil and testis, in a 66 year old man. Tonsil. x 594. Fairly uniform cells with large vesicular nuclei, finely dispersed chromatin, one or more well-defined nucleoli. Several mitotic figures in each field.



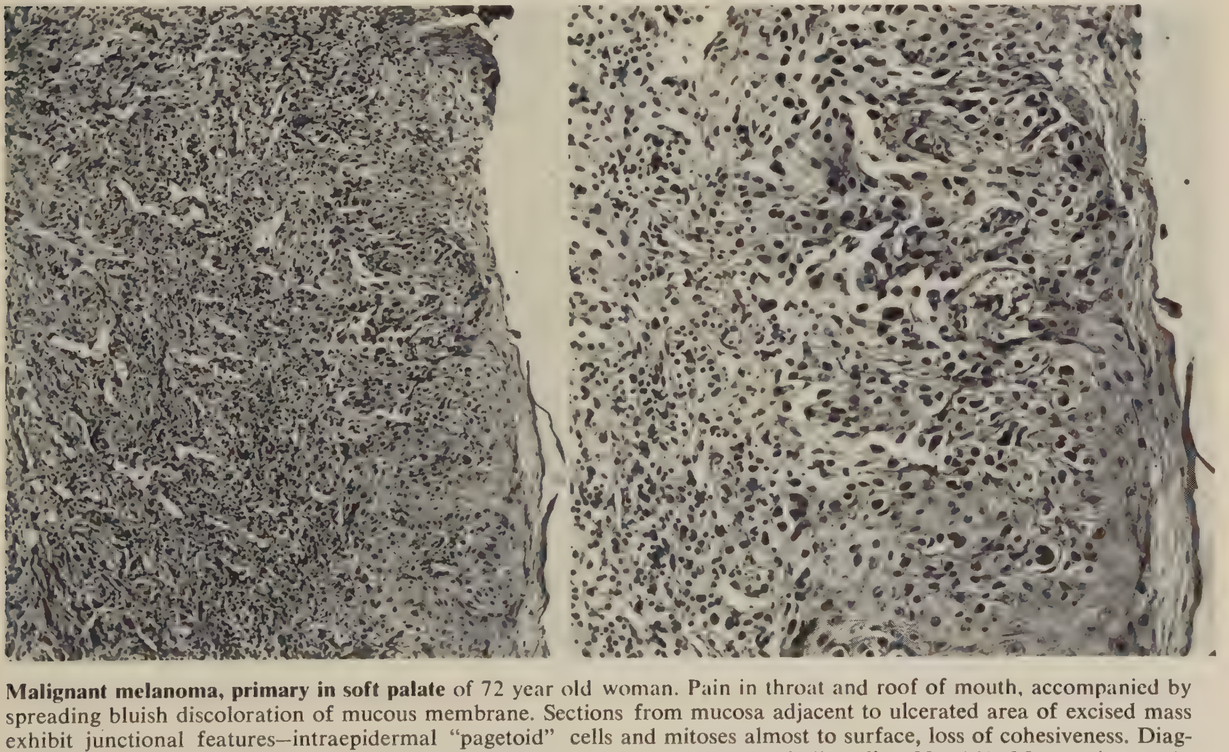
Hodgkin's disease, manifest primarily in nasopharynx of a 35 year old white man. Later confirmation by lymph node biopsy. *Left:* cellular infiltration and thickening of nasopharyngeal mucosa with preservation of some glandular structures. x48. *Right:* prominent hyperplastic reticulum cells with vesicular nuclei and prominent nucleoli; numerous lobated and giant forms (at bottom). Plasma cells, lymphocytes and eosinophils also evident. x610.



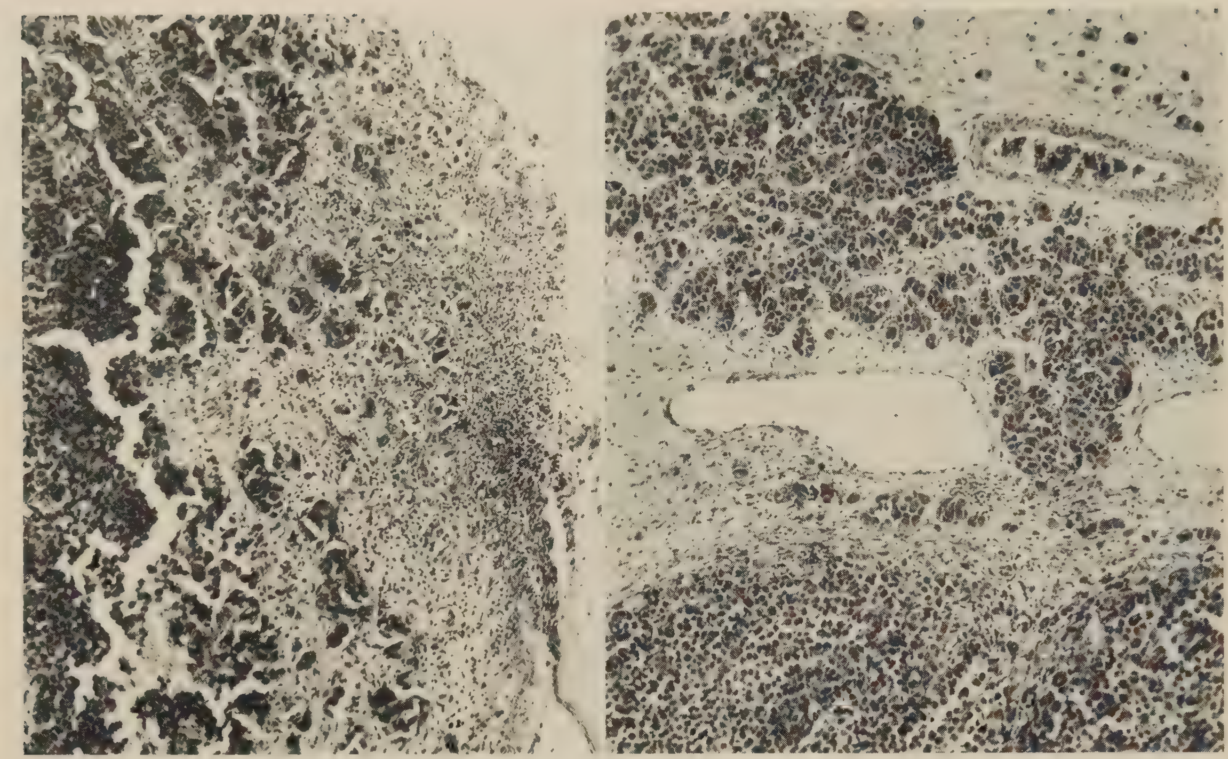
Hodgkin's disease initially manifest in nasal cavity of a young man. **A.** Polypoid, partially necrotic fragments of tissue resected. x14. **B.** Granulomatous lesion with areas of necrosis initially diagnosed granulomatous inflammation though large malignant reticulum cells and atypical mitoses were very frequent. x48. **C.** Lobated Reed-Sternberg cell in center; atypical mitosis at bottom. Polymorphous cellular infiltrate. x590. (R.E. Johnson, Columbia, Mo.)



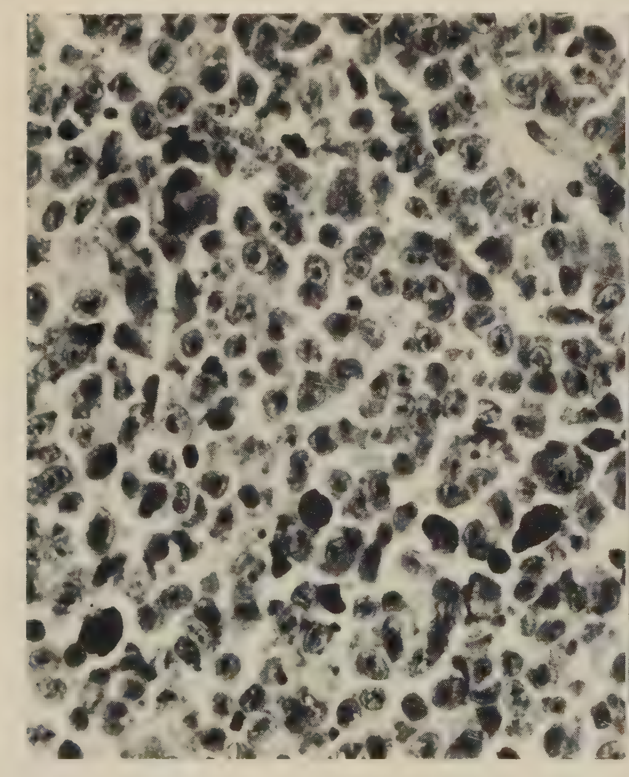
Malignant melanoma, primary in maxillary sinus, of a 63 year old woman. Preoperative diagnosis: maxillary sinusitis. Six months after operation sinus was filled with dirty gray tumor. Patient died a year after first operation. Liver metastasis was found at laparotomy. **A.** Masses and tubules of small nevus cells in primary tumor. Overlying respiratory epithelium not involved in this field. **B** and **C.** Cellular, actively growing tumor with large, bizarre forms, from second operation. Little pigment evident. (H. Brady, Philadelphia.)



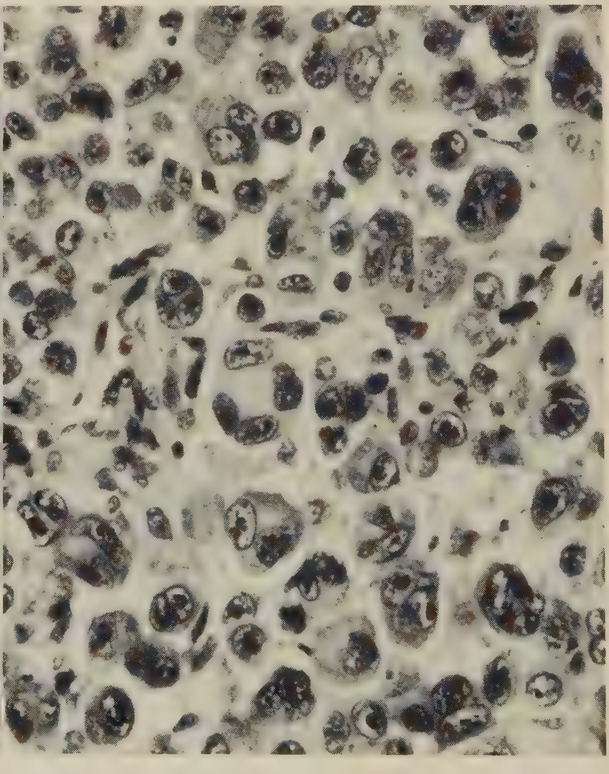
Malignant melanoma, primary in soft palate of 72 year old woman. Pain in throat and roof of mouth, accompanied by spreading bluish discoloration of mucous membrane. Sections from mucosa adjacent to ulcerated area of excised mass exhibit junctional features—intraepidermal "pagetoid" cells and mitoses almost to surface, loss of cohesiveness. Diagnosis was obscured in large area of the tumor composed of undifferentiated spindle cells. x88, x160. Metastasis to subauricular lymph nodes. (J.S. Forrester, Harrisburg, Pa.)



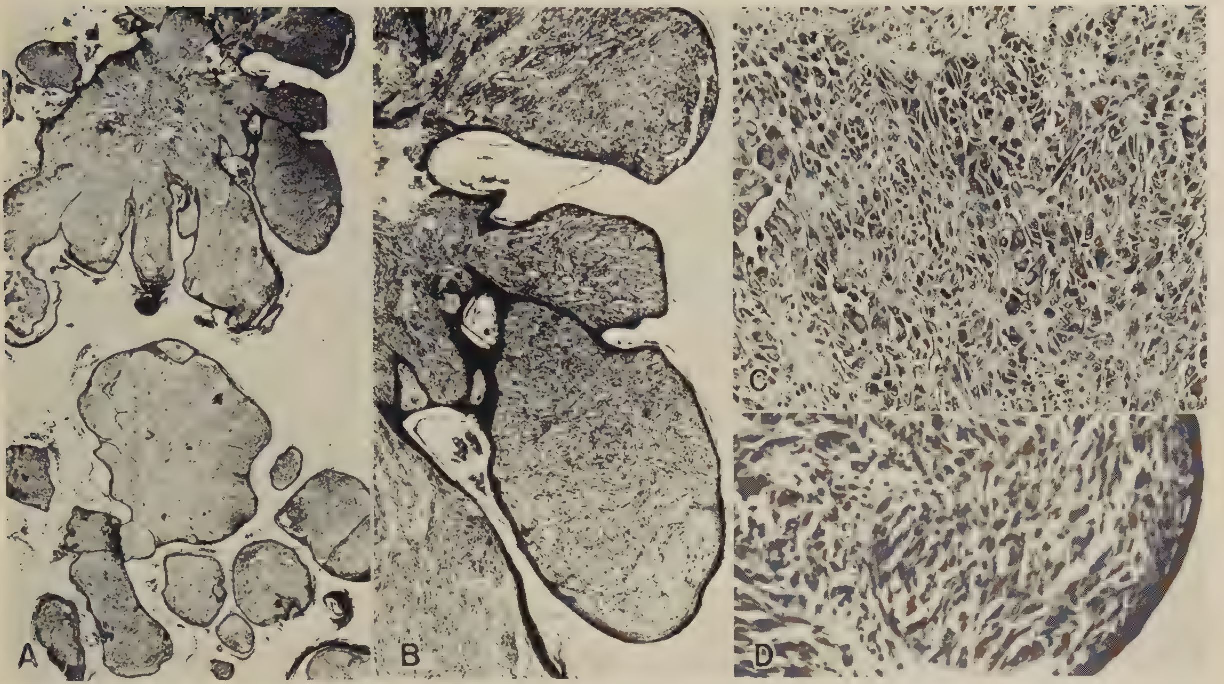
Malignant melanoma, nasal septum, in a 72 year old woman. Large tumor removed and base cauterized, seven months before a recurrent tumor was treated by excision and radium. Tumor appeared on opposite side of septum, and the patient died one year after the first operation. No apparent metastasis. Alveolar nests, cords, and diffuse groupings of neoplastic cells in both fields. *Left:* surface ulceration. x100. *Right:* better preserved portion of tumor. x75.



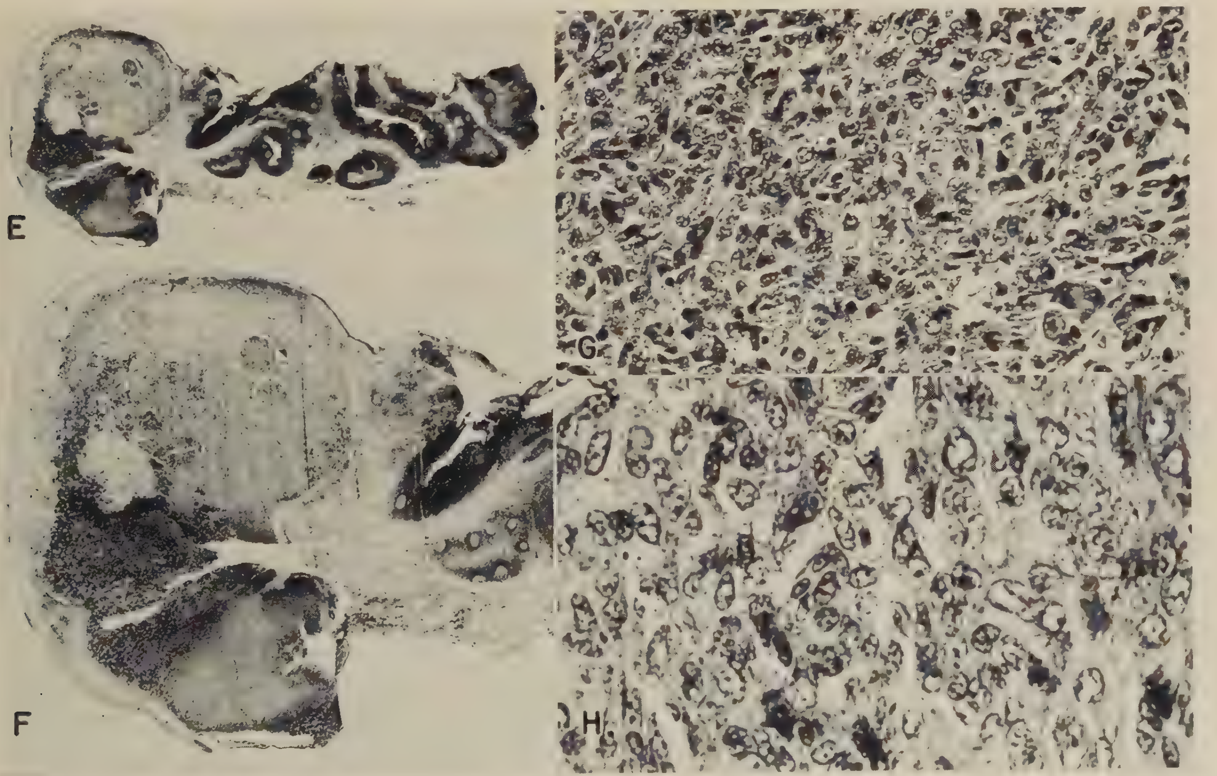
Uniform cellular structure in this tumor—round or polyhedral cells with large, vesicular, prominently nucleolated nuclei. Few heavily pigmented cells. x250.



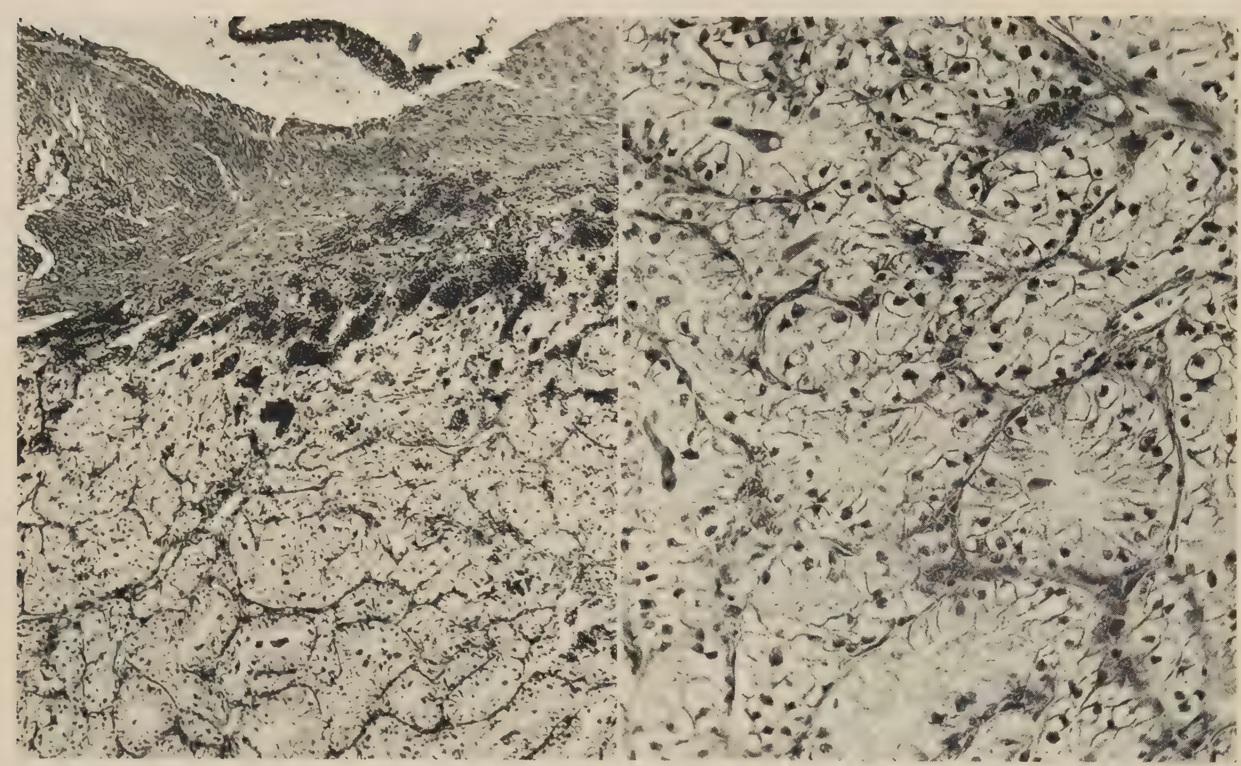
Numerous tumor giant cells are spherical, oval, or polyhedral; contain nuclei identical with mononucleated forms. x355. (L. Ostrow, Rock Island, Ill.)



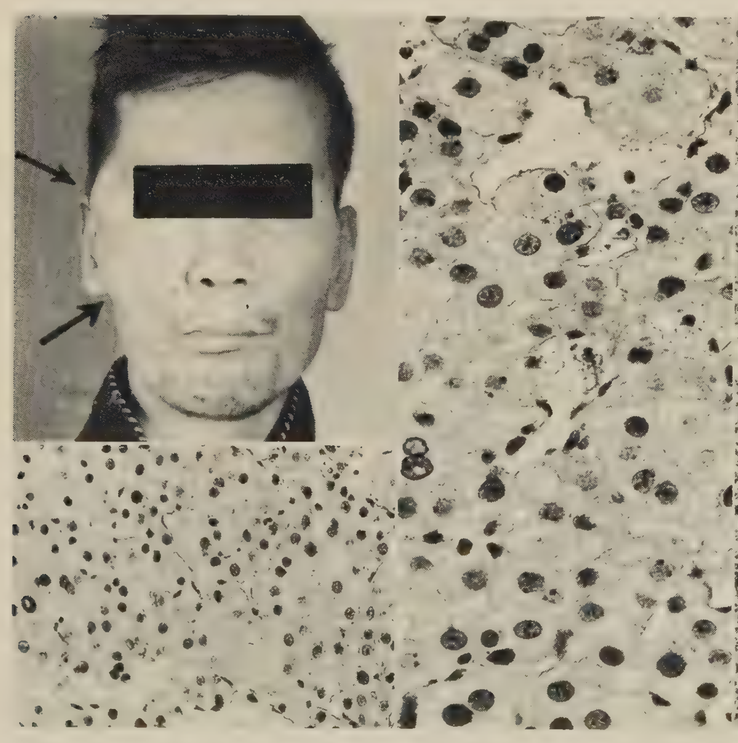
Juvenile melanoma, nasal vestibule, of an 8 month old infant. **A** and **B.** Papillary and polypoid, densely cellular lesion with numerous whorled spindle cell areas. **C.** Large numbers of characteristic giant cells. x125. **D.** Histologic features of malignant melanoma. x160. (M. Baker, Akron, Ohio.)



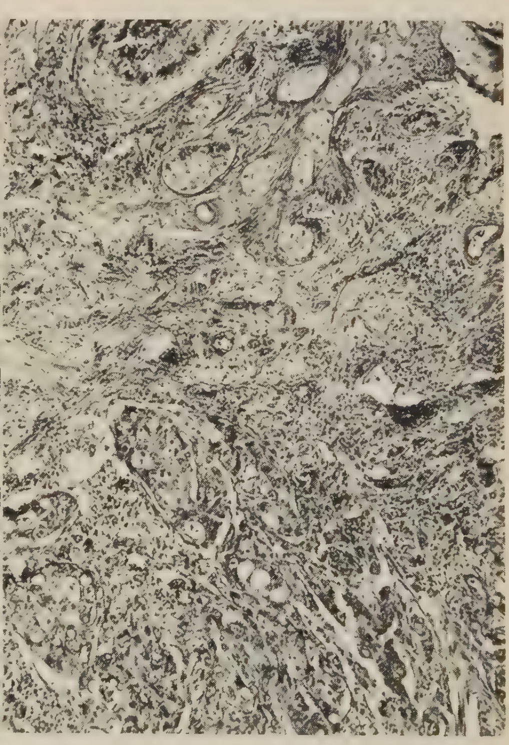
Metastatic malignant melanoma of tonsil, primary in skin. **E.** and **F.** Large tumor, lower portion of which is heavily pigmented, occupies one pole of tonsil. x2½, x7. **G.** Field in heavily pigmented zone with rather finely dispersed particles of melanin in all cells. x235. **H.** Moderately pigmented zone; variation in size and shape of cells; numerous mitoses. x400. (E.W. Townsend, Mountain Home, Tenn.)



Nasal metastasis of clear-cell adenocarcinoma of kidney caused obstruction and bleeding. The small encapsulated renal tumor was demonstrated by x-ray. The patient died 10 months later of massive involvement of bones of skull. The metastatic growth is typical tubular clear-cell tumor. x 83, x 285.



Hepatoma, metastatic to maxillary sinus and zygoma *(arrows)*. Curettings from sinus show typical liver-like cells of hepatoma. x 160, x 440. Primary tumor of liver found at autopsy. (J. A. Kirchner, New Haven, Conn.)



Adenocarcinoma, cardioesophageal junction, metastatic to ala of nose. Moderately well differentiated invasive tumor with mucus-secreting cells. Sebaceous glands of skin above. x 83.

CHAPTER 22

TUMORS ARISING IN BONE

Tumors arising from osseous tissue and its "accessories" are of particular importance because of their tendency to involve the bones of the face and skull.

Ossifying Fibroma. – Whether this is actually a neoplasm or a clinical variety of fibrous dysplasia of bone is undetermined. The maxilla is its site of predilection and very early in its development it comes to occupy the maxillary sinus. It is a nonmalignant, expansile growth, beginning as replacement of the fatty marrow by cellular fibrous tissue that retains a certain amount of osteogenic ability. The normal trabeculae are replaced by this slow-growing fibrous tissue, and eventually in this tissue new trabeculae of bone are formed. Parts of the tumor may have different proportions of bony trabeculae; some areas are more cellular, others more collagenous, and there are areas of giant cells of the osteoclastic type. These are all features that can be found in fibrous dysplasia of bone as has already been discussed in Chapter 6.

There is also a question as to whether **nonosteogenic fibroma** of bone is a separate entity. The histologic differentiation is the absence of osteoid, but the pattern of the connective tissue is identical with that of fibrous dysplasia, and furthermore lipoid histiocytes and osteoclastic giant cells are usually present. The current tendency, however, is to separate as entities these lesions from fibrous dysplasia.

Giant cell tumor, as it affects the mandible and maxilla, particularly the latter, is of two types. The first is the peripheral giant cell tumor that occurs on the alveolar process of the maxilla and arises from the periosteum or periodontal membrane. This is the clinical epulis. The second is the central giant cell tumor which occurs chiefly in regions of endochondral ossification, the symphysis of the mandible and the alveolar process of the upper jaw. There is still controversy as to whether this is in reality a neoplastic lesion or a reaction to bone injury. The tumor as seen in the maxilla, although benign, has definite neoplastic characteristics. It invades the maxillary sinus early, fills it, and by pressure extends into the orbit, nose, and cranial cavity. Other sites for giant cell tumor are the ends of the long bones, particularly the lower end of the femur and the upper end of the tibia.

It is not possible to differentiate the tumor by symptoms or x-ray appearance from other neoplasms, such as ossifying fibroma, that originate in the maxilla and invade the maxillary sinuses. The tumor rather obviously arises from osteogenic elements and the giant cells that characterize the tumor, therefore, are osteoclasts. Willis, in fact, calls the tumor osteoclastoma.

Early symptoms of giant cell tumor arising in the alveolar portion of the maxilla are frequently the loosening and extrusion of teeth and the enlargement of the alveolar process. The tumors that arise in the mandible are more sharply outlined, are cystic in character, and may be mistaken for bone cysts or cystic ameloblastomas. In general, they are tumors of young adult life. Following extraction of a tooth involved in such a process, tumor tissue rapidly fills the defect and mushrooms into the mouth. Such a case is included in the illustrations in the section on inflammation.

Microscopically, the giant cell tumor has a richly vascular background of spindle cells of fibroblastic character. The cells are plump with well defined nuclei which are generally uniform in size and contour. The characteristic feature is the large number of multinucleated giant cells. These are masses of irregularly shaped cytoplasm containing many nuclei, generally grouped away from the periphery of the cytoplasm. They resemble the nuclei of the stromal cells and are uniform in size and shape. The giant cells are frequently in intimate relationship with blood vessels, at times forming a portion of their walls. In malignant variants of the giant cell tumor the nuclei are usually fewer in number and of varying size, shape, and chromatin content.

The tumor injures the normal bone trabeculae by pressure and the cortex of the bone may be destroyed. The tumor will then invade the contiguous space or tissue. There is no evidence of osteogenesis in the tumor itself.

The presence of giant cells is not a sufficient criterion to permit designation of the lesion as giant cell tumor. It is necessary to appraise the histologic and clinical aspects, including the blood chemistry, to differentiate it from other bone lesions in which giant cells of the same type are found. These lesions include reaction of bone to injury or infection, fibrous dysplasia, and osteitis fibrosa cystica.

These tumors are benign in the strict sense, but unless they are removed in the early stages they may be clinically malignant because of the difficulty of eradicating them surgically or by irradiation. The case illustrated in the following plates is one in point: exophthalmos and nasal obstruction called attention to a tumor in a 70-year-old Negro. The tumor grew expansively, eroding the right orbital plate of the ethmoid, filling the nose on both sides, and eroding the cribriform plate of the ethmoids and extending into the cranial cavity.

Osteoid-osteoma, first identified by Jaffe, has occasionally been described in the bones of the skull, including the nasal bones. It arises from osteoblastic mesenchyme and is characterized by a large amount of osteoid tissue. Portions of it may become calcified, but such calcified trabeculae, instead of being separated by vascular stroma and other elements of bone marrow, mix with the osteoid tissue which contains numerous osteoblasts. It is a tumor of young adolescence. It is a benign tumor and does not invade the soft tissues.

Myeloma. — The extramedullary plasmacytoma, encountered in the soft tissues of the upper respiratory tract, is the rarer form of this tumor. The intraosseous form, either as a solitary lesion without demonstrable involvement of other bones or as a part of the more usual multicentric disease, is seen in the bones of the skull, especially in the cranium. The mandible is more frequently the site of the tumor than the maxilla.

Myeloma is a central tumor of bone causing areas of rarefaction, and in any form it is a tumor of the older age group. If the tumor is a solitary one of the mandible, maxilla, or temporal bone, it is impossible to differentiate it, except by biopsy, from the other rarefying lesions; but if it is part of the multicentric tumor, a survey of the skeleton will establish this fact and be important evidence in the differentiation. The lesions are usually round. When the calvarium is involved, there is a characteristic mottling in the roentgenogram. The Bence-Jones protein is usually demonstrable in the urine when the tumor is in the bone, but is absent when the tumor is extramedullary. There is also a marked increase in the total blood proteins and a reversal of the albumin-globulin ratio.

The histogenesis of the tumor is not clear, but then neither is the origin of the plasma cell itself definitely established. Tumors including other elements of the bone marrow, lymphocytic, myeloid, or even erythroblastic, have been grouped with the myeloma, but by far the commonest are those in which the plasma-cell type can be identified. It is doubtful that the other rarer bone-marrow tumors should be included with the myeloma.

The prognosis in the multicentric tumor is invariably bad and death usually occurs in a few years. But if the tumor is solitary and can be completely removed, there is a possibility that it will not recur. This is contrary to the experience with extramedullary plasmacytomas. After complete removal there is no assurance that years later the intra-osseous phase of the tumor will not develop.

Extramedullary plasmacytoma has been discussed in the previous chapter.

Ewing's Tumor of Bone. — While this tumor of childhood most frequently affects the long bones of the extremities, several have been encountered in the maxilla and mandible.

There is some dispute as to its histogenesis. Ewing interpreted it as a myeloid tumor derived from endothelium; but, while it is generally acknowledged as a definite entity primary in bone, it probably arises from the reticuloendothelium of the bone marrow. It apparently does not arise from osseous tissue, because it never shows the osteogenic properties of tumors arising from that specialized tissue.

The several examples, in the Registry, of the tumor arising in the bones of the face, all from young children, have grown with remarkable rapidity. The first evidence is usually trouble with a tooth. An x-ray will then reveal an area of rarefaction in the surrounding bone, generally with involvement of the periosteum. The soft parts are quickly invaded and death usually results in a matter of months. Under these circumstances death occurs before metastasis becomes evident, but the tumor arising in its usual site, the long bones, does metastasize freely, especially to the lungs.

Histologically, the tumor consists of sheets of small, round or slightly spindle-shaped cells growing on a support of delicate, well vascularized connective tissue stroma. The outline of the individual cell is obscured by the close packing. Mitotic figures are plentiful, but variation in the cell size and shape and giant cells are not seen as in other malignant bone tumors. It resembles most closely the tumor of sympathetic nerve origin—sympathicoblastoma. The latter, however, shows the characteristic rosette arrangement of cells, an important differentiating feature. Ewing's tumor also grows more consistently about the blood vessels, and portions of the tumor more remote from the blood vessels are necrotic.

Ewing's tumor is highly sensitive to irradiation, but this form of treatment, like surgical procedures, has proved ineffectual in curing the tumor as it occurs in the jaws of children.

Reticulum Cell Sarcoma of Bone.—The reticulum cell sarcoma of the soft tissues, particularly of the lymphatic elements of the upper respiratory tract, is of much more importance than the rare tumor of bone. In this latter situation it is closely allied to Ewing's tumor, in fact, many tumors that have been reported as of the Ewing type proved later to be of reticuloendothelial origin. It is like Ewing's tumor in that it occurs principally in the long bones, but it is occasionally seen in the bones of the jaws. It produces the same roentgenographic changes and it is sensitive to irradiation. It differs from Ewing's tumor in that metastasis apparently occurs much later, so that complete extirpation of the primary tumor by surgical means or by irradiation can effect a cure.

This tumor shows no osteogenic properties and it occurs in an older age group than does the Ewing tumor.

Microscopically, the pleomorphic endothelial-like cells have more cytoplasm than do lymphocytes. By special stains reticulin fibrils can be demonstrated in close association with the tumor cells. The cells do not show the fascicular grouping usually seen in the Ewing tumor. The differentiation from the Ewing tumor is important because of the difference in prognosis.

Metastatic tumors in the bones of the face are relatively rare, but it is surprising how frequently in the Registry material the first evidence of such a tumor has been a loose tooth. A warning more appropriate for the dentist than for the otolaryngologist, it emphasizes the suspicion with which every loose tooth must be approached. The metastatic tumors have included melanoma, malignant tumors of the lymphatic tissue series, and the sympathetic nerve cell tumors, primary in the abdomen of children. Carcinoma, however, is the most common secondary tumor of the mandible and maxilla, occurring as a direct extension of tumors primary in the neighboring mucosa, particularly of the gingiva and the floor of the mouth. Carcinomas of the prostate and the breast occasionally metastasize to the jaws.

ODONTOGENIC TUMORS

It is not necessary to go into detail concerning this group of lesions, but it is important that the otolaryngologist have a working knowledge of them because some of them, particularly the ameloblastoma and certain of the cysts, may invade his field. Any of the bone lesions, but especially the cysts, may be evident in routine roentgenologic surveys of the face and jaw.

Cysts of the Jaws.—Aside from the bone dysplasias that present as cystic lesions, there are several cysts that occur in both jaws. These fall into three general groups: 1, those that arise in connection with the tooth buds; 2, those that are the result of developmental defects during the fusion of the maxillary and nasal processes; 3, the radicular cysts which develop at the ends of and occasionally along the tooth roots.

The cysts that arise from the tooth bud elements and thus are possible in either jaw are called FOLLICULAR CYSTS. The follicular cyst develops in the enamel organ by an accumulation of fluid in the stellate reticulum. The cyst may reach large size and usually prevents the eruption of the tooth. This is an important differentiating feature. It possesses a fairly dense capsule and partially surrounds the body of the tooth.

The RADICULAR CYST is the commonest cyst of the jaws and develops at the tips of the tooth roots, less commonly along the root—lateral radicular cyst. It is lined by granulation tissue or by squamous epithelium which comes from rests (debris of Malassez) that are always present in the periodontal membrane. This is the most important of the cysts to otolaryngologists because it can break through the thin floor of the maxillary sinus and be confused with sinusitis both clinically and roentgenologically. Such a case is included in the following illustrations.

The developmental cysts include: 1. The MEDIAN PALATINE CYST which occurs in the midline of the maxilla just behind the central incisors or farther back in the palate. It results from the inclusion of epithelium from the mucosa of the mouth in the median fissure during fusion of the palatal processes. It can attain considerable size and appears in the x-ray as a typical heart-shaped vacuolation in the midline of the upper jaw. The cysts occurring farther back on the palate are lined either by the squamous epithelium of the mouth or by the respiratory epithelium of the nose. The cyst expands so as to cause bulging of the palate into the oral cavity.

2. The NASOPALATINE CYST occurs in the incisor canal and is the remains of the nasopalatine ducts, which, in the embryo, communicate between the nose and the mouth. The ducts may persist as a fistula opening into the mouth just to one side of the anterior median line of the palate. Histologically, the cyst is lined by either squamous or respiratory epithelium and at times contains mucous glands.

3. The GLOBULO-MAXILLARY CYST results from inclusion of epithelium at the point where the globular and maxillary processes fuse to form the upper jaw. It is between the upper lateral incisor and cuspid teeth, so that when it expands, it pushes the roots of these teeth apart. This feature distinguishes it from the simple radicular cyst. These cysts are lined by squamous epithelium.

Any of these cysts may, by expansion, bulge into the floor of the nose or less commonly into the antrum. The nasopalatine cyst is the one most likely to involve the nose, because it may develop in the nasal end of the nasopalatine duct. The reinforcement to the floor of the nose furnished by the nasal septum resists invasion of the centrally located median alveolar and median palatal cysts. House reported 48 cysts of the maxilla that were treated by radical surgical procedures. Twenty-four had invaded the maxillary sinus.

Ameloblastoma (adamantinoma) is derived from the epithelial portion of the tooth follicle. Although this is the portion that forms the enamel of the tooth, the tumor never shows mature enamel. It may arise from the formed tooth bud or from fragments of epithelium remaining from the dental lamina. This is the extension of the surface epithelium into the alveolar ridges from whch tooth buds develop.

The tumor is most commonly found in the mandible at the junction of the body and the ramus. It is a tumor of middle life and more frequent in the male. It is a central bone tumor and may not manifest itself until it has expanded and deformed the bone. Although metastases have been described, it is essentially a benign tumor.

The tumor is of two types, solid and cystic. There may be a solitary cyst or multiple cysts, but in all tumors of any size there will be at least microscopic cysts because of degenerative changes in the epithelial masses.

The epithelial portion of the tumor is characterized by elongated and branching groups of cells, the outer layers of which are columnar and palisaded like the enamaloblast of the developing tooth, and the centrally located ones, star-shaped like the stellate reticulum of the normally developing enamel organ. These cell masses are surrounded by connective tissue stroma which in the young tumors is highly vascularized.

The cyst develops by the accumulation of fluid in the centers of the cell masses; this gradually expands the groups of cells and flattens the epithelium until eventually the cysts become lined by a single layer of flat or cuboidal epithelium which is not identifiable as ameloblastic.

At times the epithelium undergoes squamous cell differentiation which may lead to a mistaken diagnosis of carcinoma. More rarely the tumor differentiates into the glandular type. In rare tumors there is melanin pigment in the epithelial cells. Complete removal is essential because any retained epithelium will continue to grow. This may be a very difficult surgical procedure, particularly when the tumor is in the maxilla and invades the antrum and nose.

Differentiation between ameloblastoma and certain other epithelial tumors that show a somewhat similar grouping may be difficult. This is particularly true of an invading mixed cell tumor of the salivary-gland type originating in the palate, and transitional cell carcinoma arising from schneiderian membrane that shows a pseudoadenomatous arrangement of the cells. In fact, Willis insists that such tumors are really ameloblastomas that develop from epithelial rests in the thin portion of the maxilla forming the floor of the maxillary sinus. This point is also mentioned in the section on malignant tumors of the nose, sinuses and pharynx.

Ameloblastomas primary in the sphenoid have been described. If accepted as such, their histogenesis could be traced to epithelium of the craniopharyngeal sinus that has retained its ameloblastic properties. It is likely, however, that this is merely another example of the ameloblastoid arrangement of the epithelium seen in some transitional cell carcinomas of the nose and sinuses.

The other solid tumors of odontogenic origin do not concern us particularly. Not only are there tumors that arise from the epithelial portion, the ameloblastoma and mature enameloma, but a series of tumors that arise from the mesenchymal portion of the tooth bud that is destined to form dentin, cementum, and pulp. Such tumors may occur with or without calcification. They are all benign and we can leave them to the oral surgeon and to the pathologist for further differentiation.

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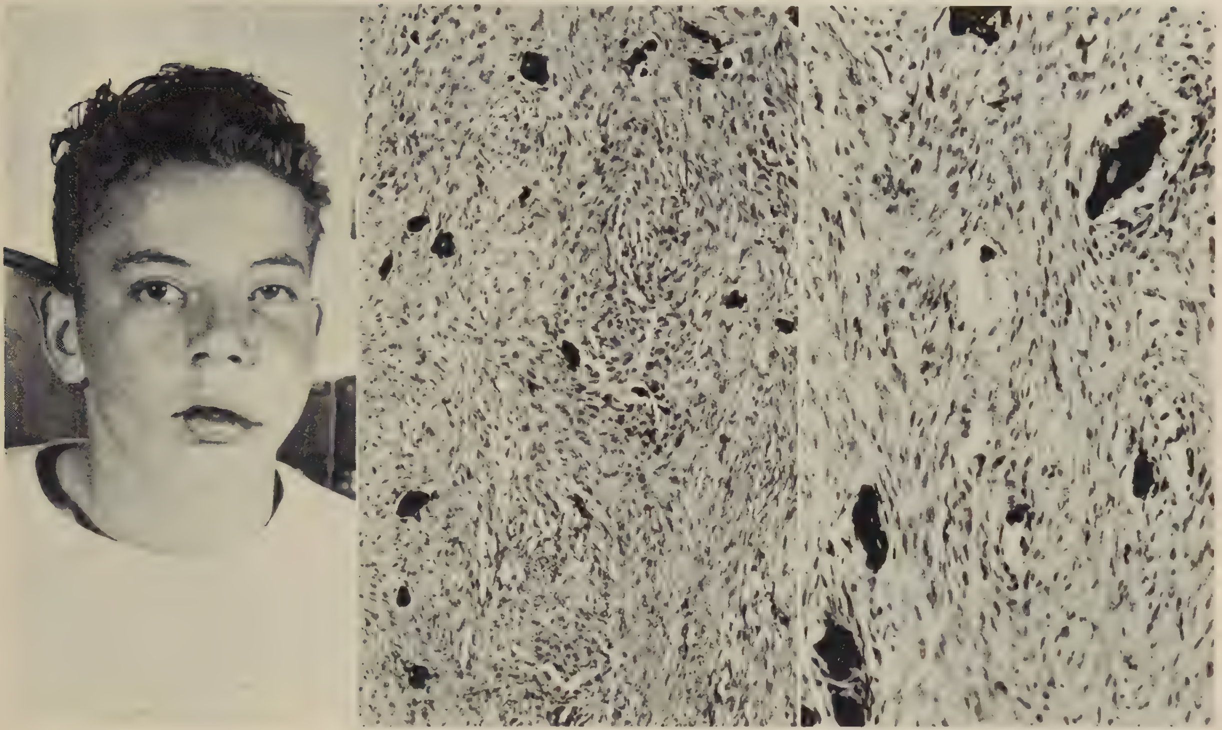
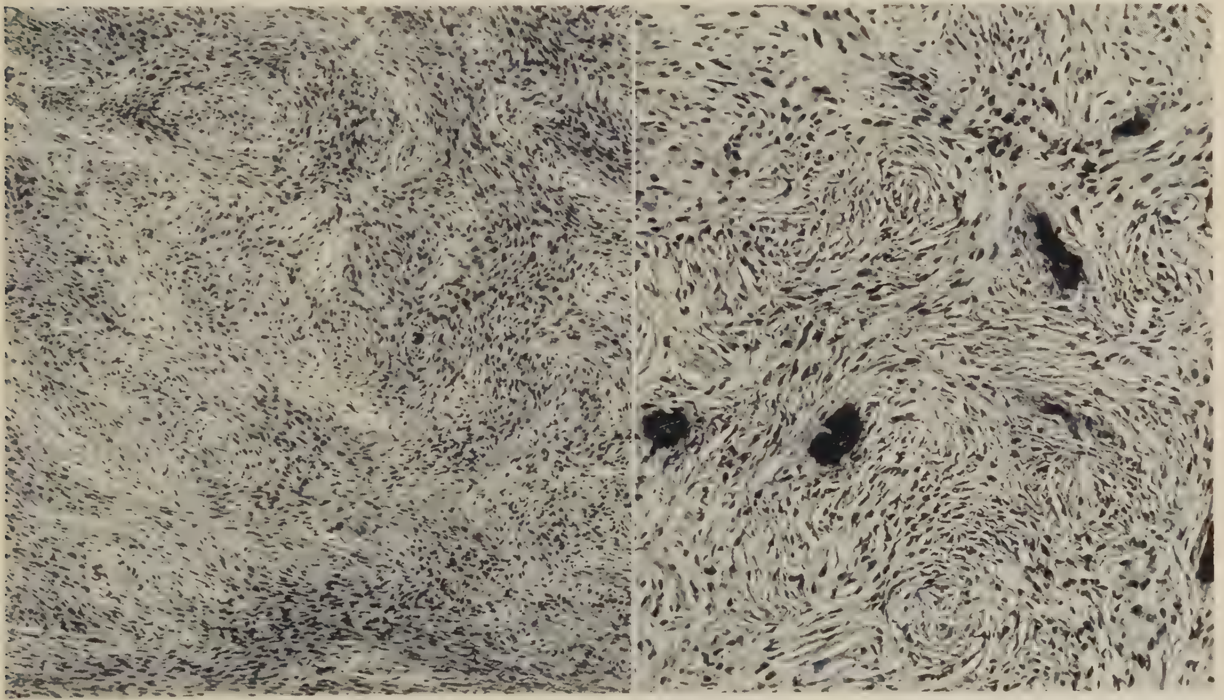
House, L. R.: Benign Cysts of the Superior Maxilla with Special Reference to Cysts of Maxillary Sinus. Arch. Otol., Rhin. & Laryng., *48*:301–326, 1948.

ENDOSTEAL FIBROMA, MAXILLA

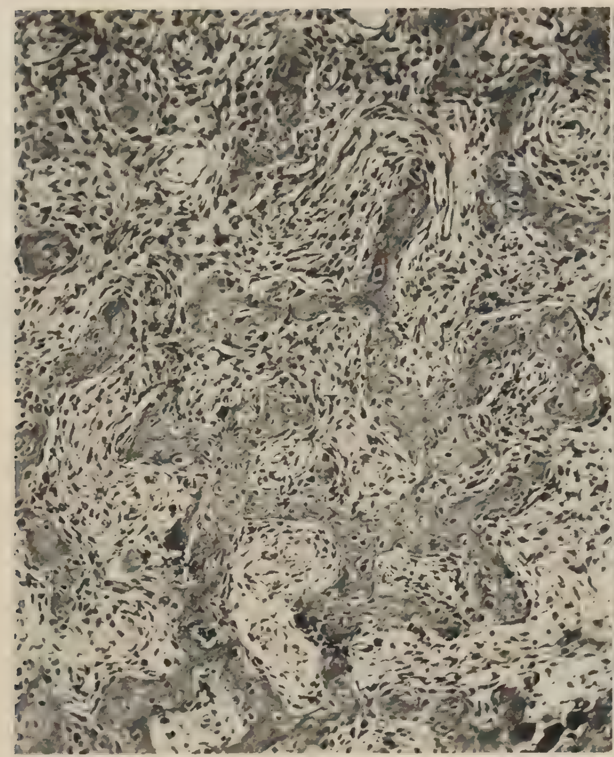
(OSSIFYING FIBROMA)



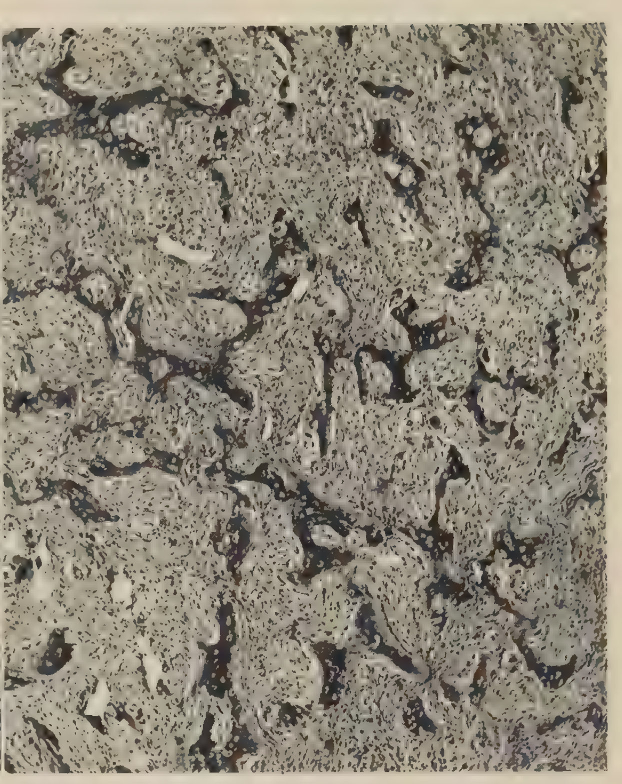
Painless swelling of the face of six months' duration, in a 16 year old boy. X-ray revealed an expansile tumor in the antrum. Well-encapsulated, firm mass removed by Caldwell-Luc operation. Dense fibrous tissue with spicules of calcified necrotic bone. If these are formed by the tumor, it as an ossifying fibroma. x 83, x 125. No recurrence 11 years after operation.



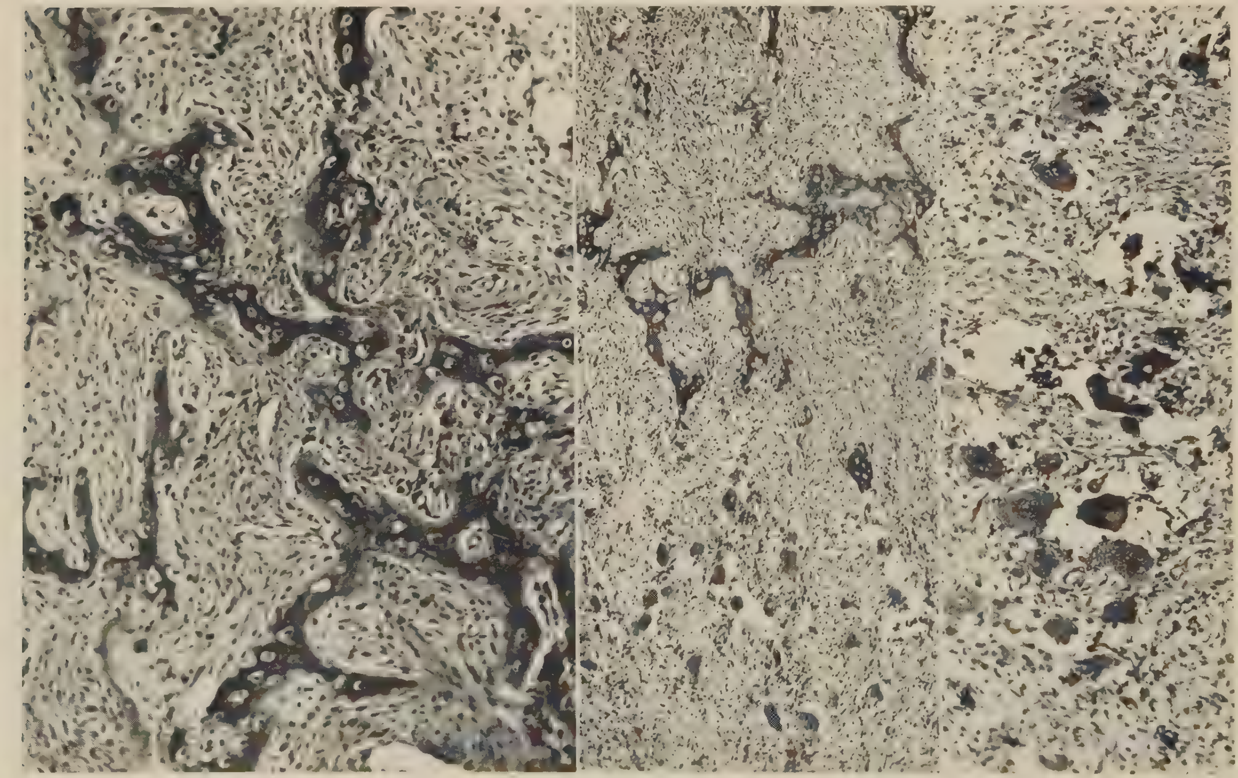
Pattern of fibrous tissue and necrotic bone is similar to that in previous case. x 83, x 125, The tumor, of 2 months' duration in a 24 year old man, occupied the antrum, eroding its lateral wall and floor, and extended into posterior alveolar ridge. No recurrence 9 years after removal by Caldwell-Luc operation.



Osteoid osteogenesis is abundant in this case. The trabeculae are outlined by a layer of osteoblasts. A benign tumor. x 125.



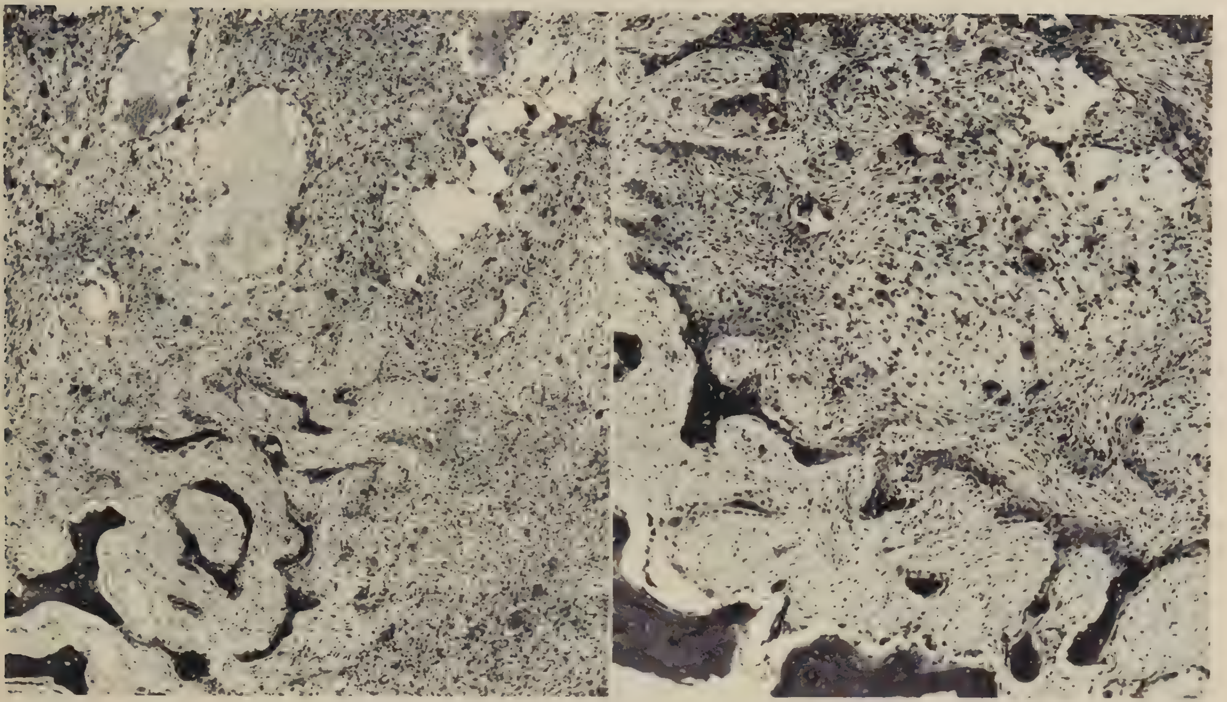
Tumor in antrum of a 20 year old man. It had been growing for six months and had produced pain, paresthesia of molar teeth, and stuffiness in nose. x 62. (Other fields below)



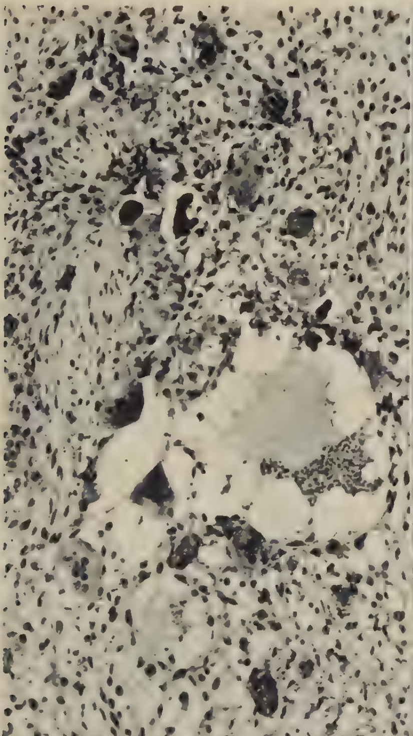
The osteoid bone is more mature than in the first case (above left) and is calcified. In other respects the microscopic appearance of this tumor differs only in the presence of foci of osteoclastic giant cells that suggest fibrous dysplasia. x 125.

GIANT CELL "TUMOR"

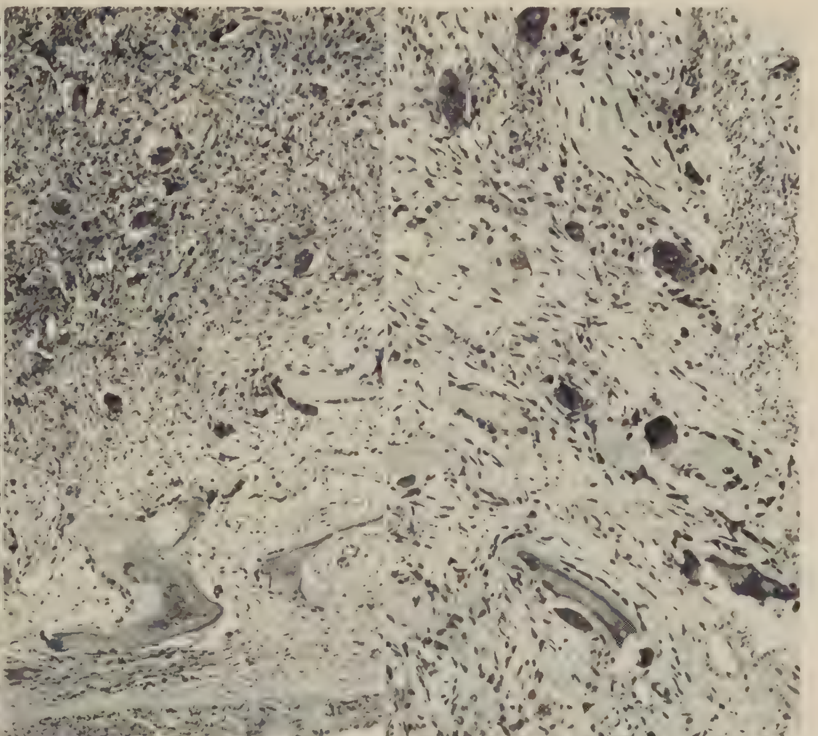
(GIANT CELL REACTIONS OR VARIANTS)



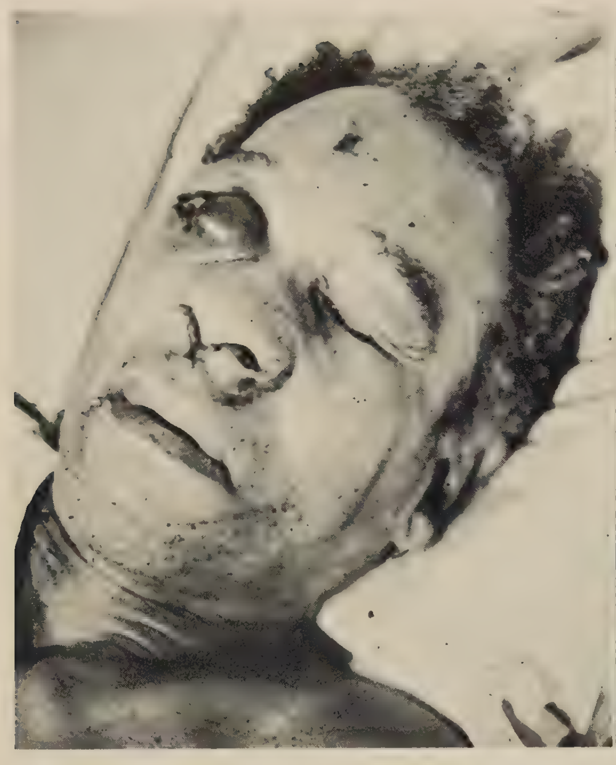
Giant cell reaction, ethmoid region, surrounded by a thin layer of bone. Background of cellular fibrous tissue with vacuoles of degeneration and groups of giant cells. x 48, x 70. The mass, clinically apparent for six months or more, was removed from the ethmoidal-lacrimal duct region of a 7 year old boy. No recurrence a year later. More possibly a reaction to infection than a true tumor.



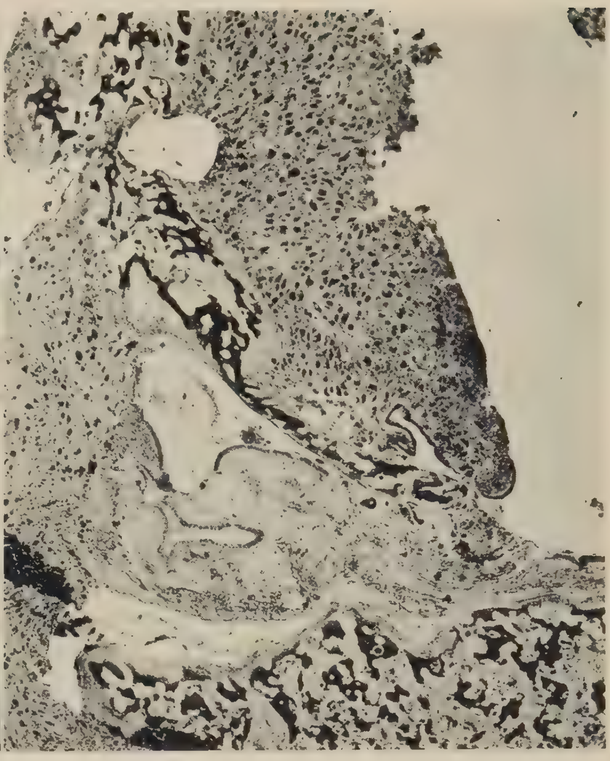
A vacuole containing polymorphonuclear leukocytes, from the case shown above. x 125.



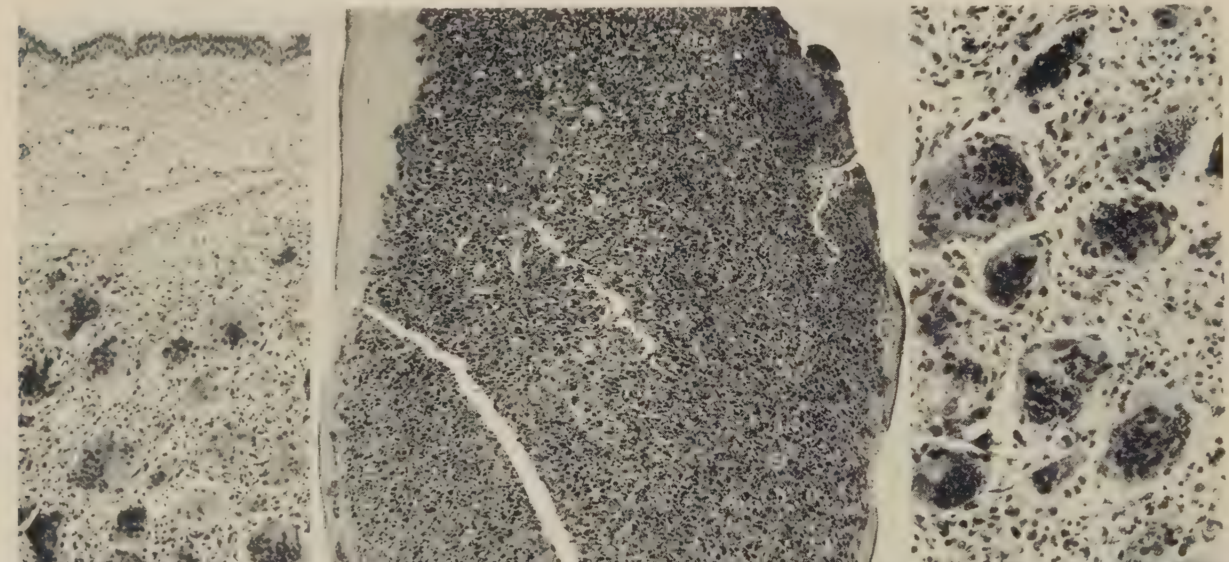
Encapsulated mass of similar appearance removed from maxillary sinus of a 33 year old man, with swelling of the face and ptosis of 3 months' duration. Orbital plate and lateral wall of sinus eroded by "tumor." Fibrous stroma, giant cells and osteoid capsule. x 114.



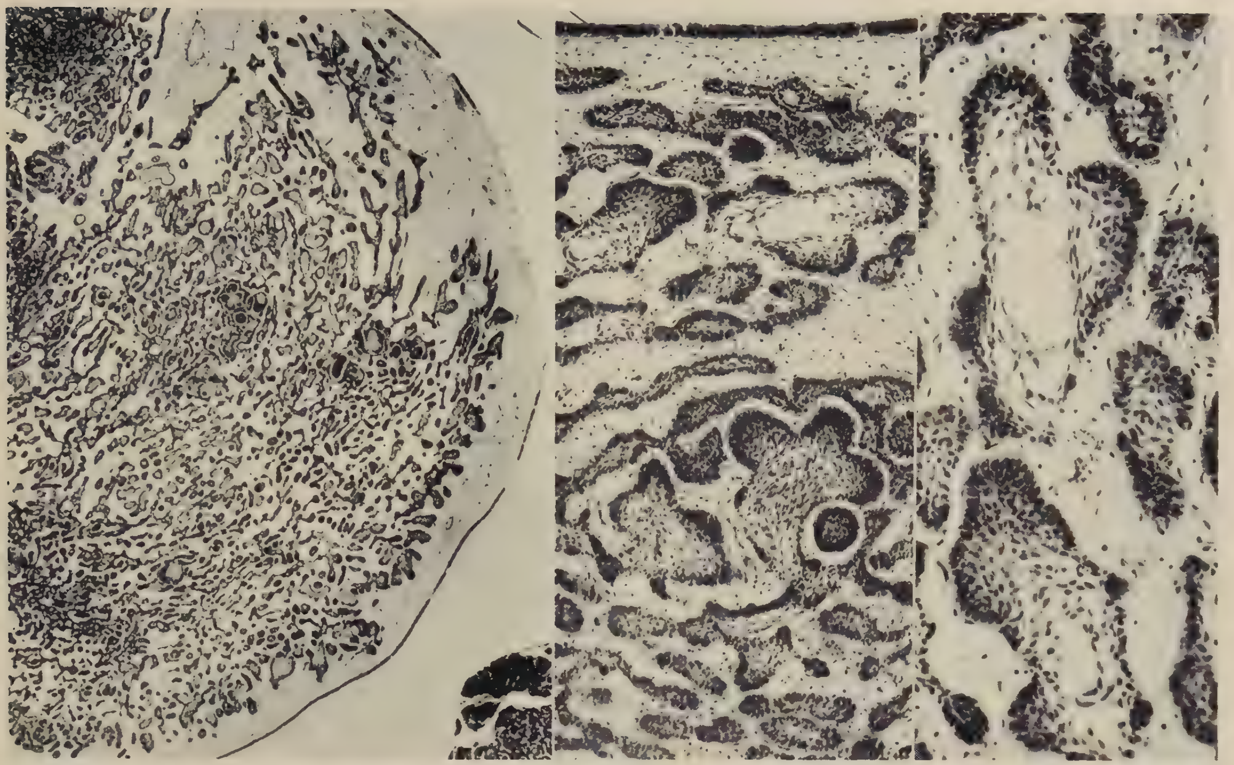
Giant cell tumor of several years' duration, evidently arising ethmoid rather than maxilla. It had eroded through cribiform and orbital plates, and filled antrum and nasal cavity (H. N. Leffler, Washington, D. C.).



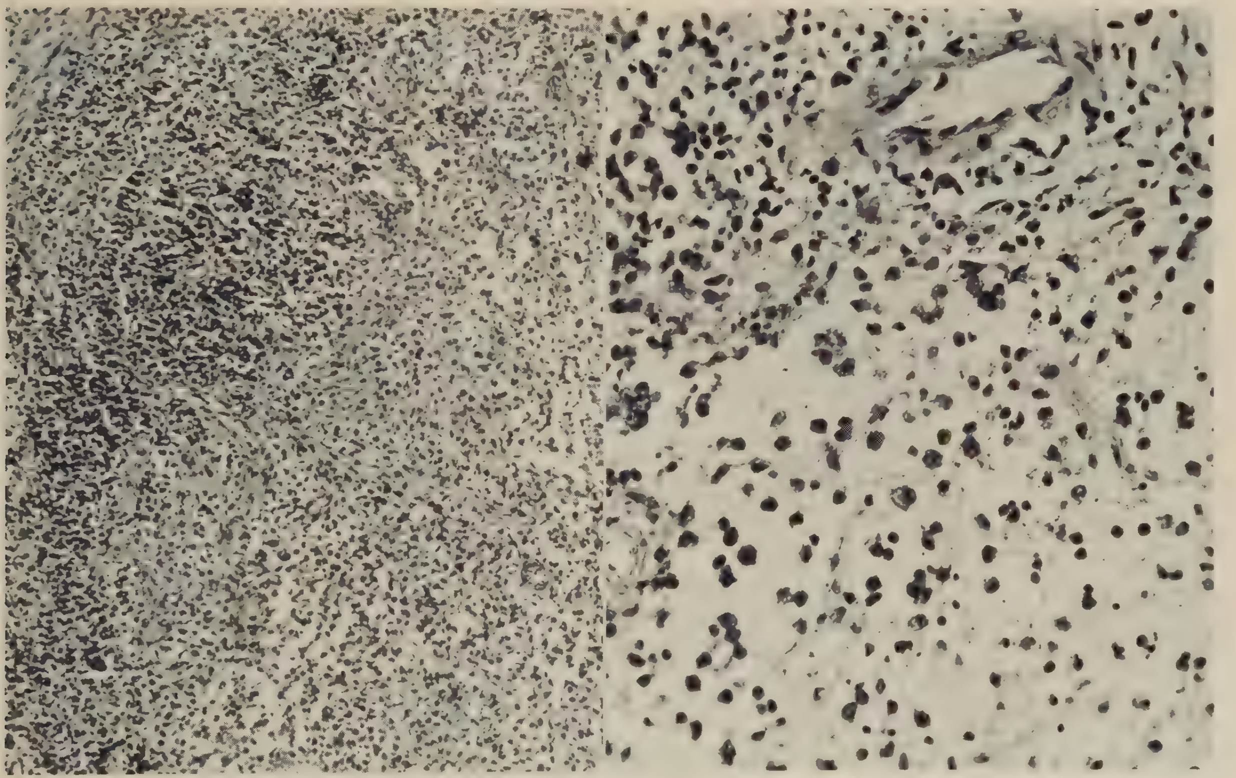
Material from ethmoid of another case in which there was x-ray evidence of Paget's disease, suggesting that like sarcoma, giant cell tumor may be a complication of that dysplasia. Tumor at top; Paget-type bone below. x 13.



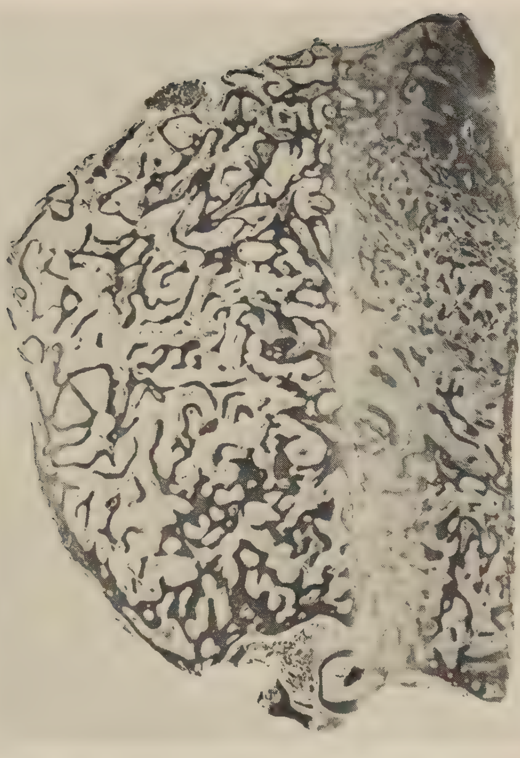
The polypoid mass (x 9), apparently arising from the ethmoidal tumor, was removed from middle meatus of the patient with Paget's disease. It is essentially a mass of osteoclastic type giant cells. Note the great number of uniform nuclei in each cell. Histologically benign. x 105, x 160.



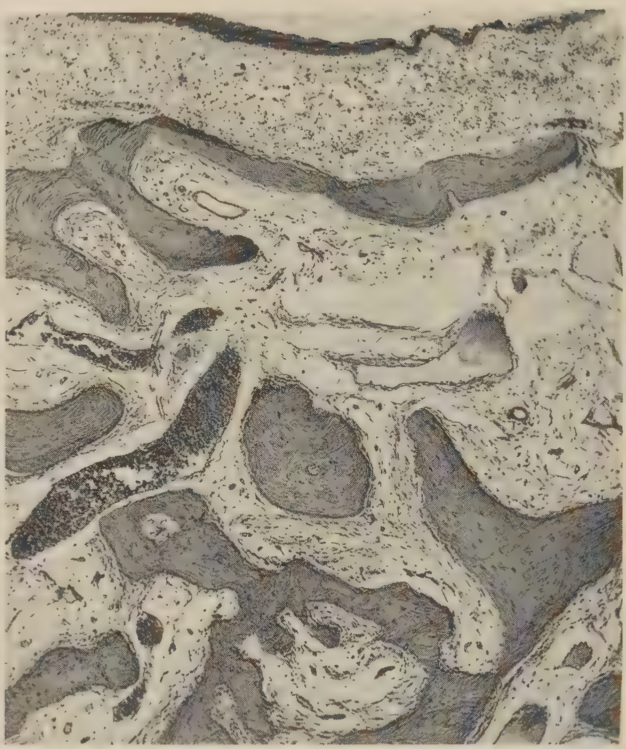
Ameloblastoma, the solid type with enameloblasts forming squamatoid borders about the stellate reticulum. x 76, x 125. This mass filled the antrum of a 52 year old man, in whom an antro-oral fistula had been present for 25 years following extraction of a molar.



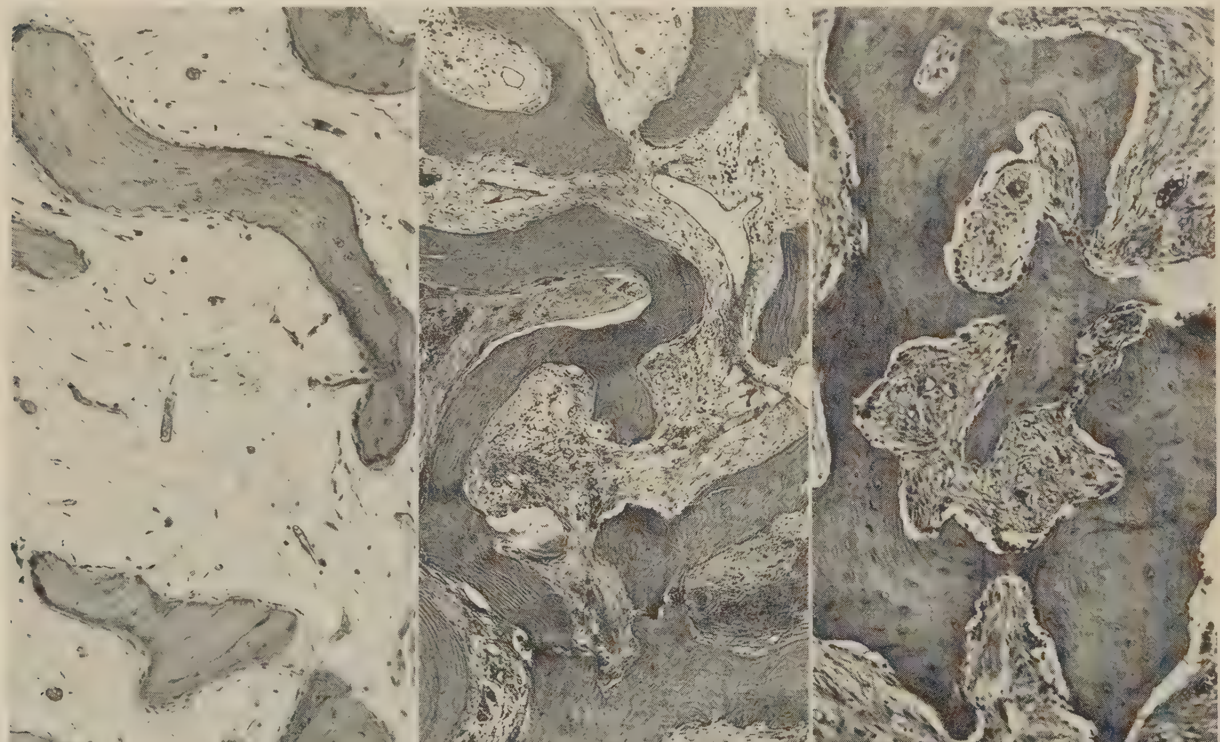
Eosinophilic granuloma removed from antrum of a 26 year old man, who had multiple bone lesions thought to be Hand-Schüller-Christian disease. Large masses of eosinophils (not recognizable as such here) and large foamy histiocytes. x 105, x 245.



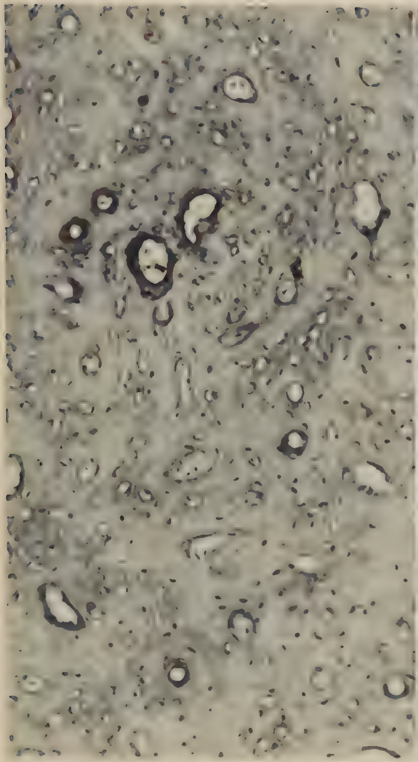
Osteoma, sinus, of dense but trabeculated bone. x 10. History of trauma or sinusitis in some of these cases suggests that the growth may be reactive rather than neoplastic.



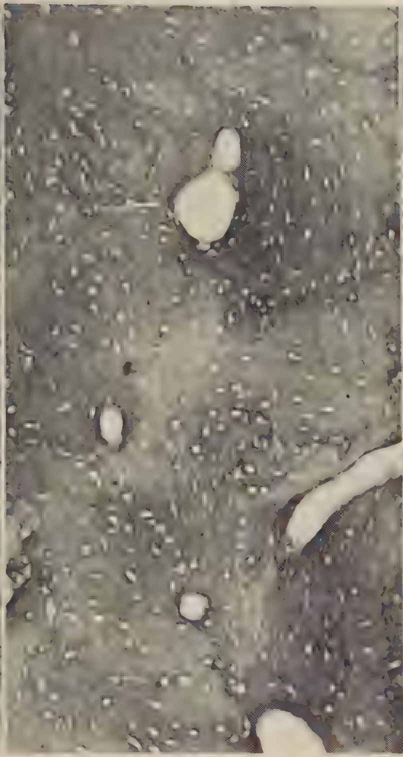
Osteoma, frontal sinus, pushing up the mucosa (at top). Vascular fibrous tissue has replaced the fatty marrow, possibly indicating an inflammatory reaction. x 48.



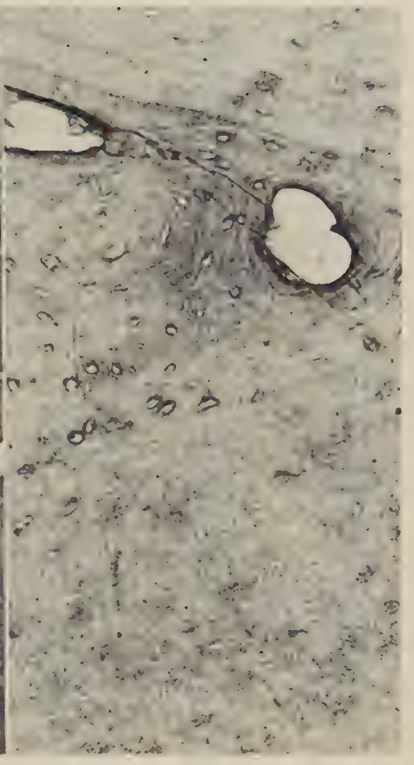
Osteoma, frontal sinus; sections of three tumors, illustrating the variation in size of bone trabeculae and in character fibrous-tissue component. x 125, x 48, x 75.



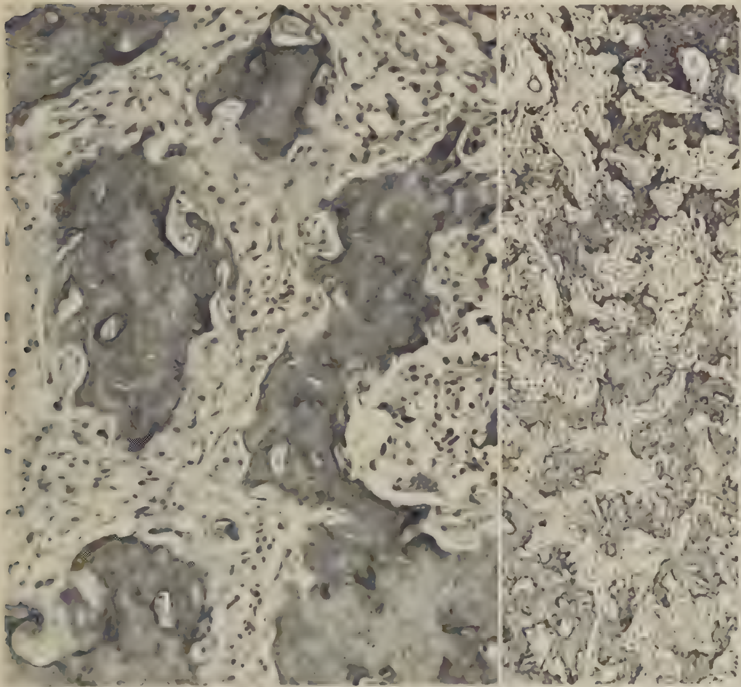
Osteoma, dense type:
In frontal sinus, extending into orbit of a 14 year old boy. x 125.



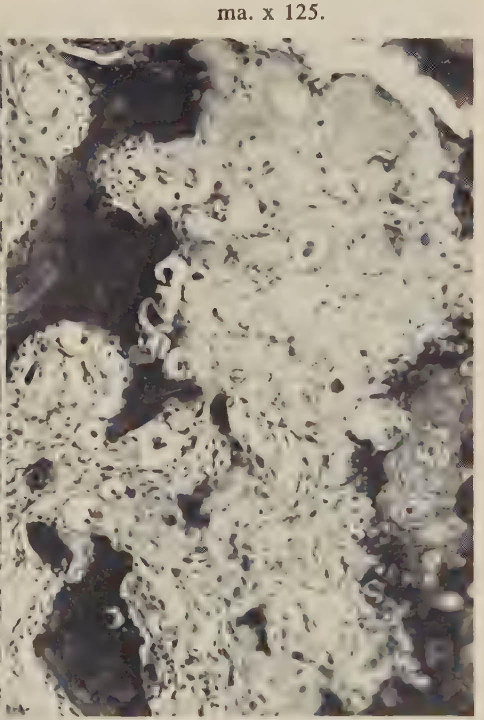
Filling frontal sinus of a 51 year old woman. Demonstrated by x-ray. x 125.



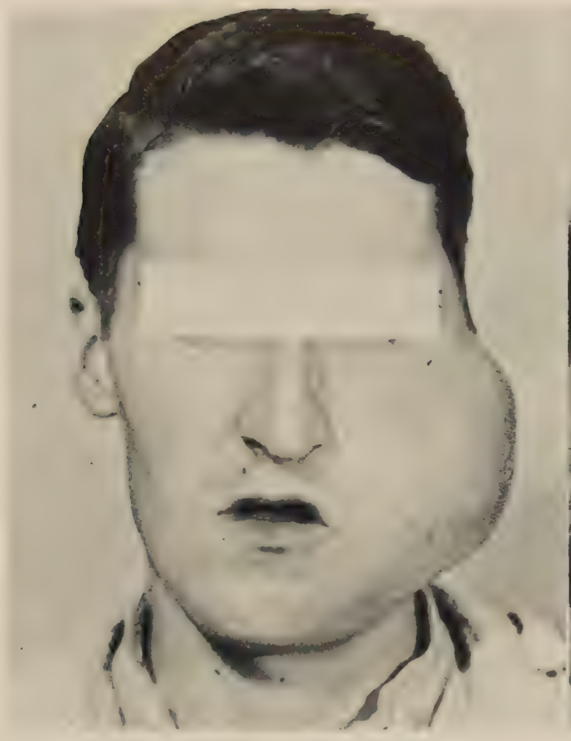
From inner table of frontal bone, a cauliflower-like growth projected into the brain of a 50 year old woman. Removed 6 years after severe local trauma. x 125.



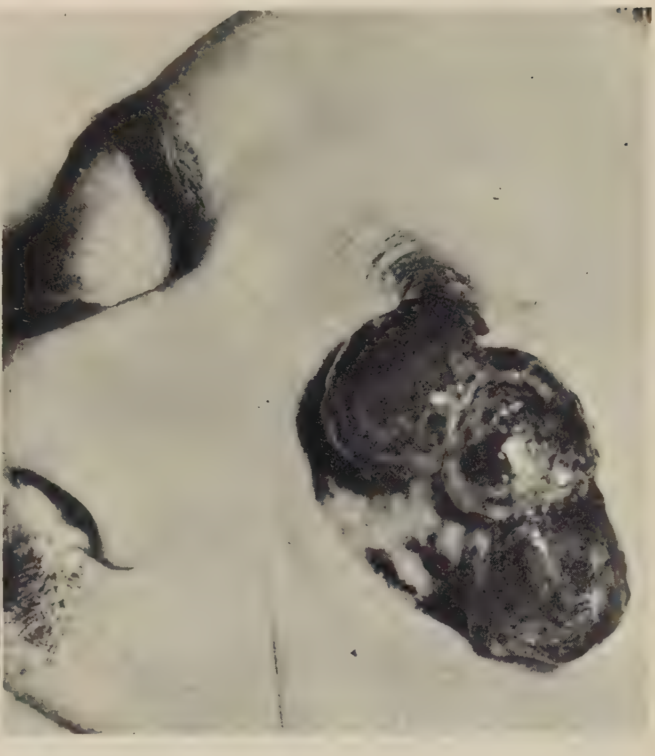
Osteoid osteoma, frontal sinus, also involving ethmoids of a 21 year old man. Headache and depression for 2 weeks. Osteoclastic as well as osteoblastic activity is evident. x 125, x 39.



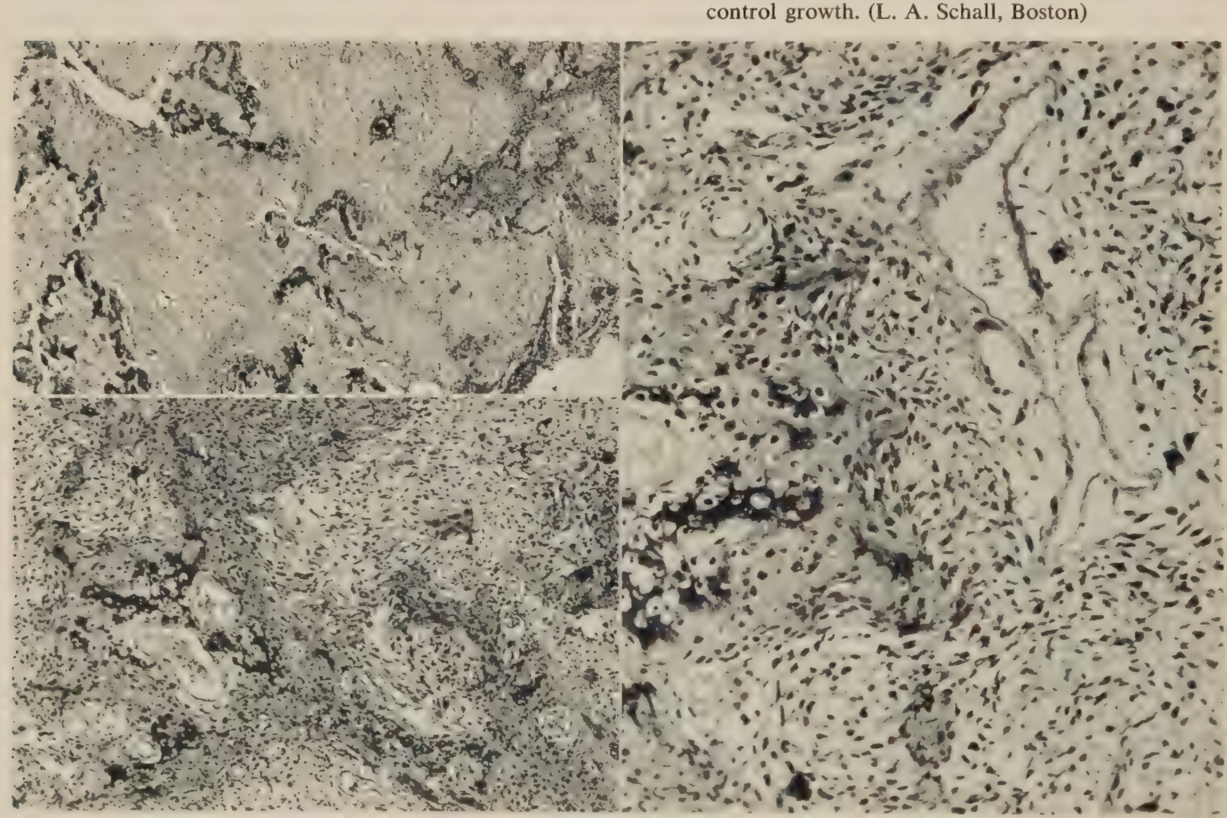
Osteochondroma, region of condyloid process of mandible. An example of enchondral bone formation. Cartilage element definitely of neoplastic type. x 125.



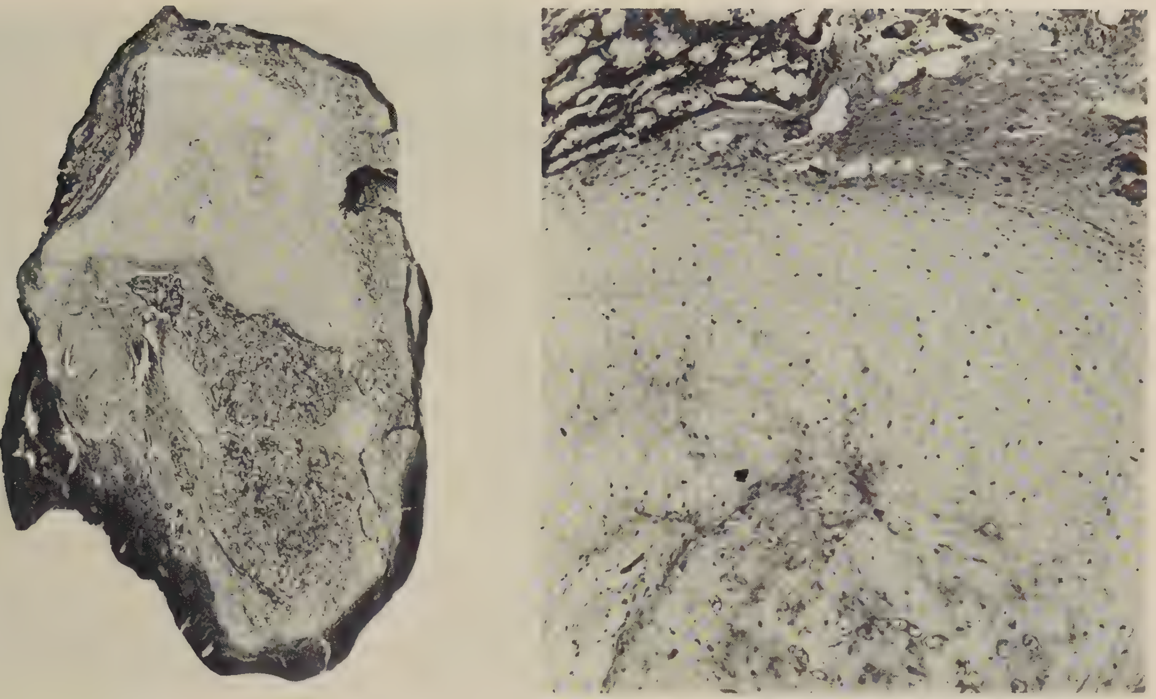
Osteogenic sarcoma, maxilla. Outcome unknown.



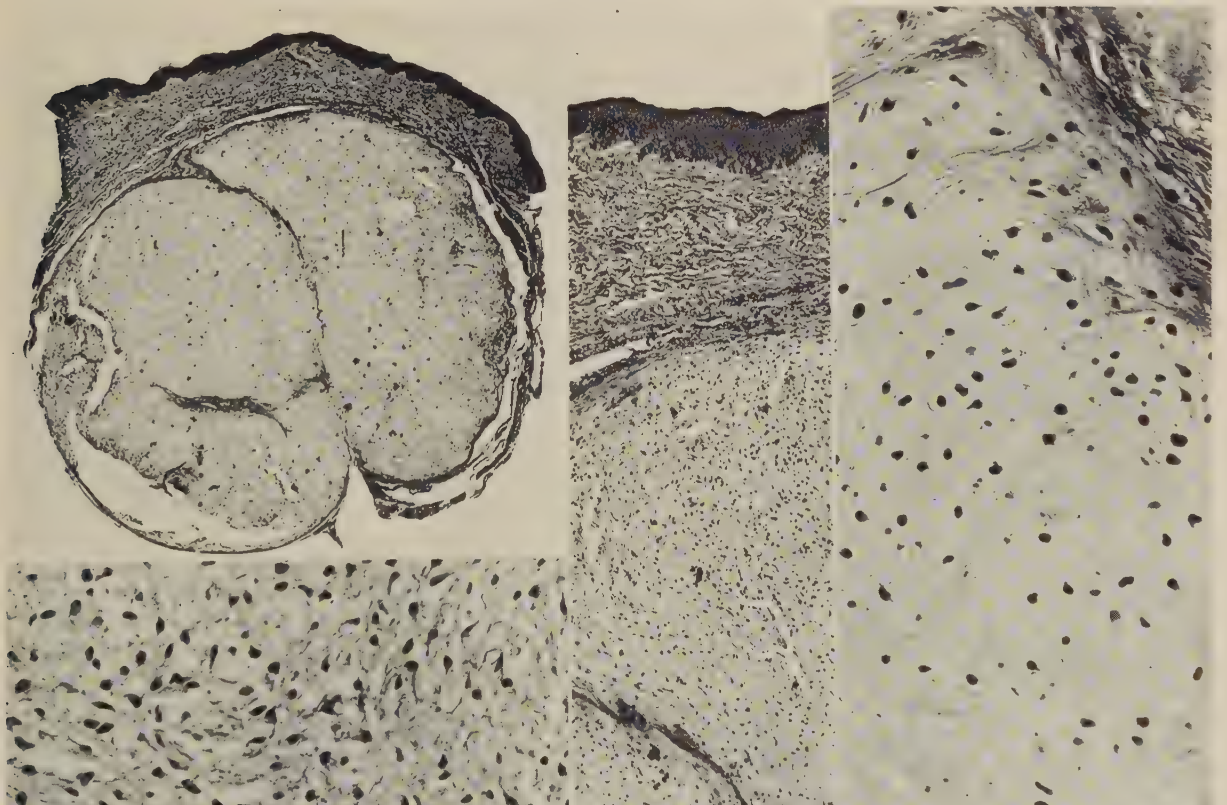
Osteogenic sarcoma, four years' duration, in a 27 year old man. Removal of maxilla and intensive irradiation therapy, followed two years later by recurrence. Exenteration of orbit did not control growth. (L. A. Schall, Boston)



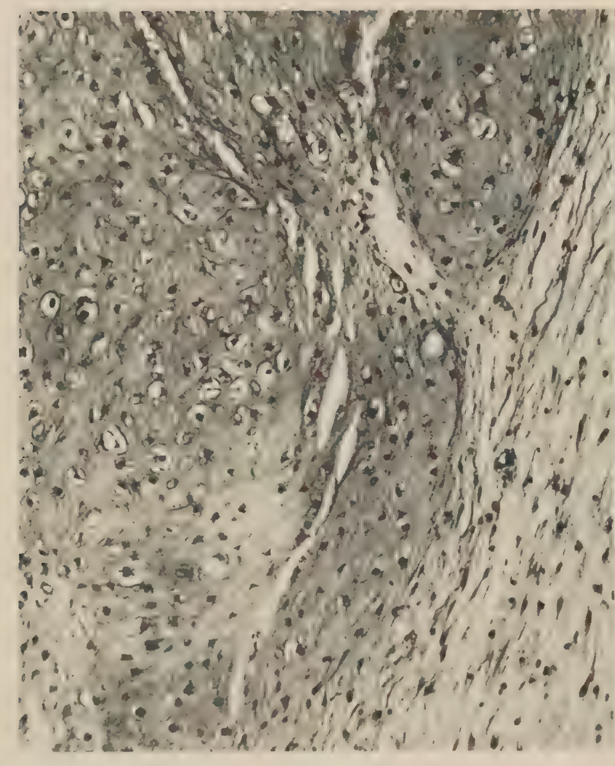
Three sections of tumor from case at right, above. Disorderly character and arrangement of osseous elements: fibrous tissue, osteoid and mature bone. The preponderance of osteoid and mature bone accounts for the relatively slow growth. x 25, x 62, x 160.



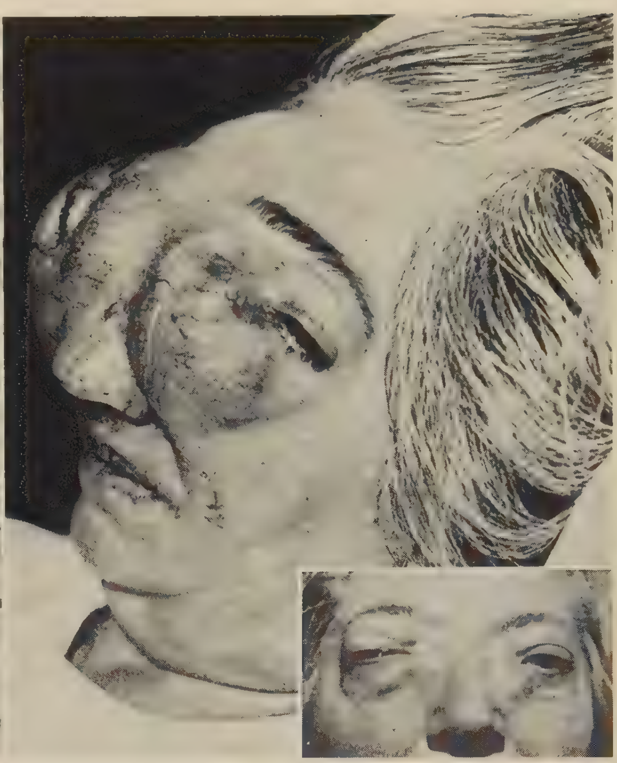
Normal eustachian cartilage (torus tubarii) from nasopharyngeal biopsy, diagnosed as chondroma. The chondrocytes have an orderly arrangement and the perichondrium is well defined.



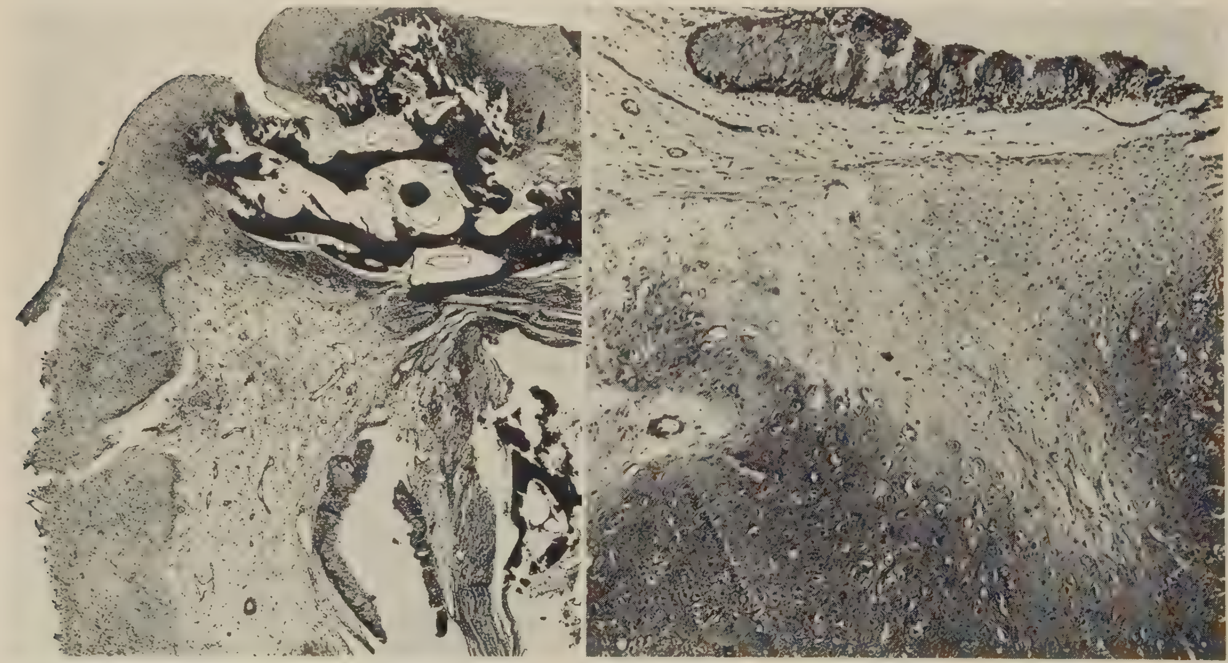
Chondroma, nasal septum, from a 9 year old girl. A. Encapsulated nodules, which enlarged progressively until removed. B and C. Fibrous portions of tumor that suggested neurofibroma. x 210, x 55. D. True cartilaginous character of tumor —chondrocytes and chondromucin matrix. x 210.



Chondroma, nose. Firm polypoid mass filling middle meatus. Well differentiated cartilage, but with chondrocytes of varying sizes in disorderly arrangement. x 114.



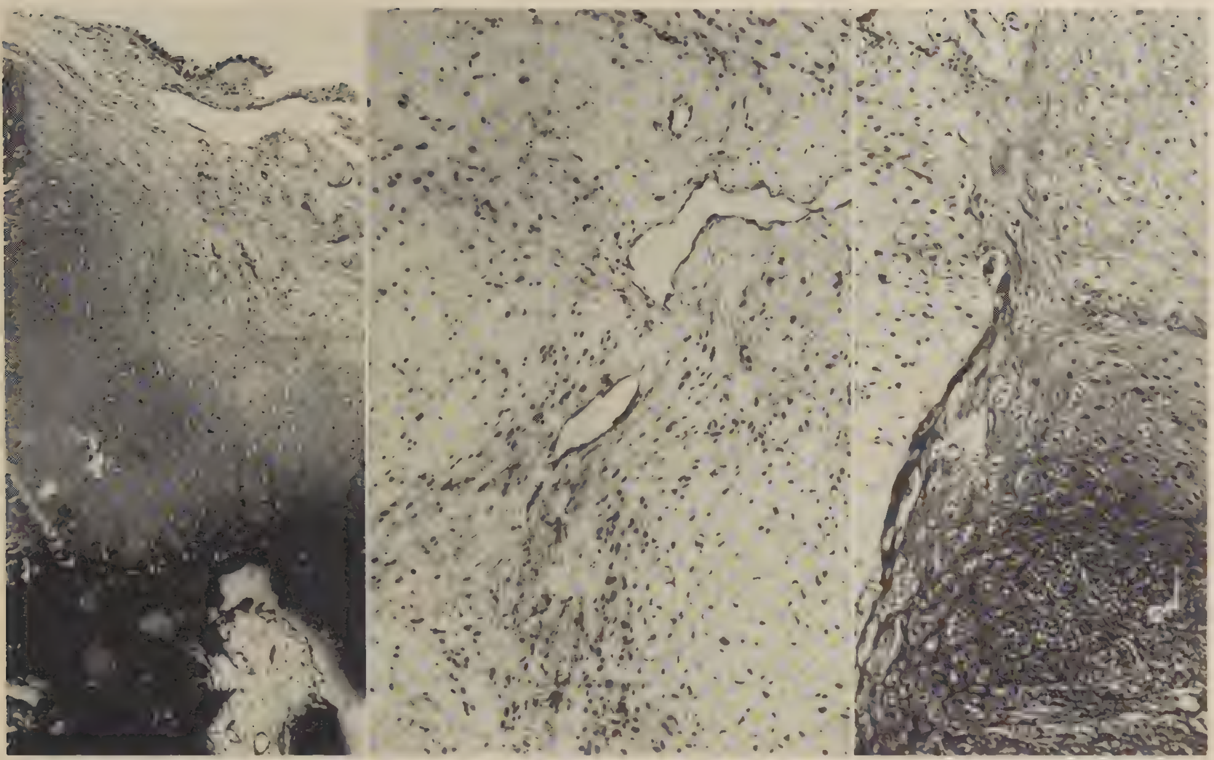
Chondrosarcoma, apparently primary in glabellar region, of long duration, several months before patient's death. Appearance several years earlier is shown in inset. Tumor extended into cranial cavity, but did not metastasize. Surgical and irradiation therapy failed to control its persistent expansion. (J. N. Ganim, Cincinnati, Ohio)



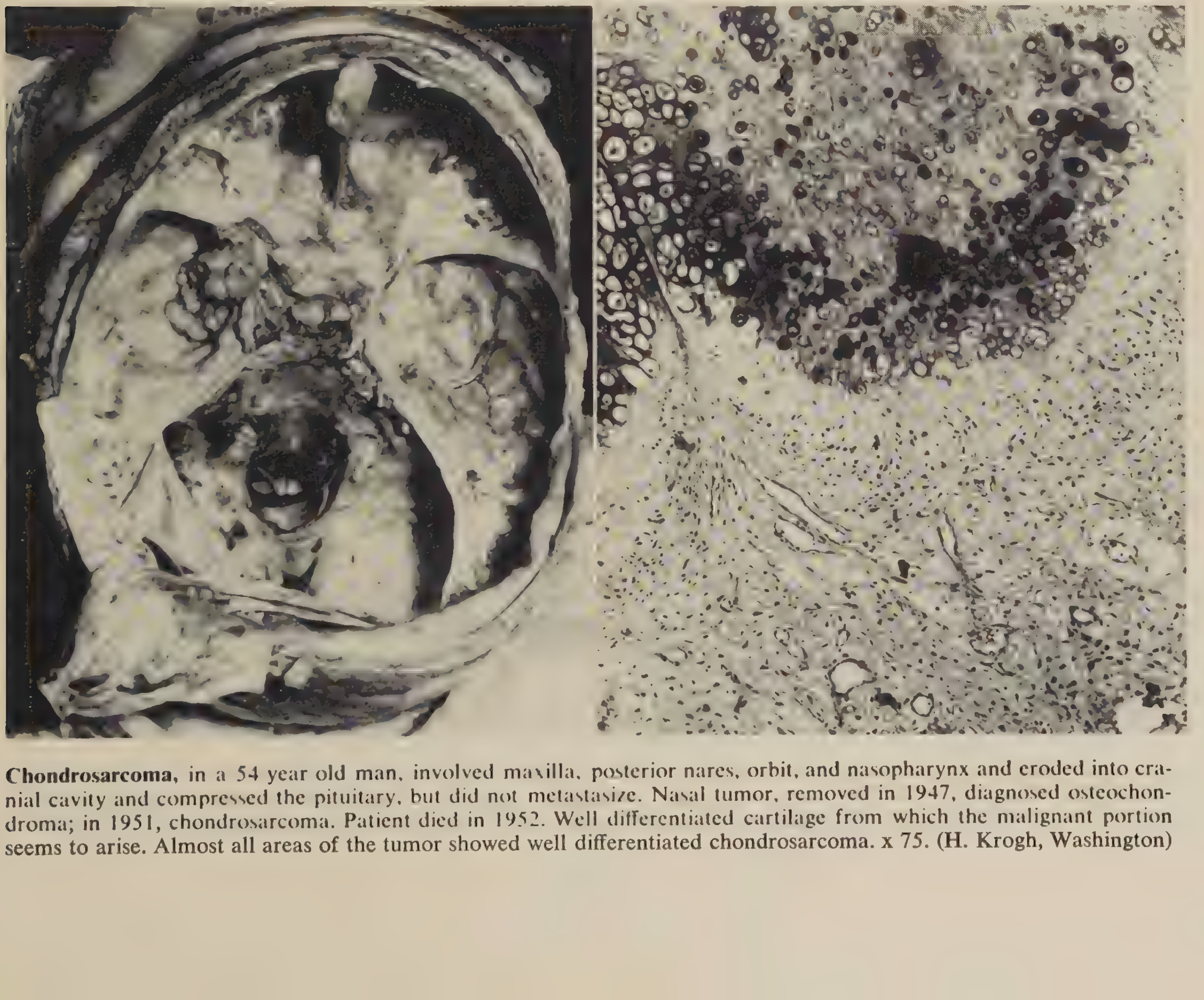
Histology of glabellar tumor:

Turbinal bone (black) being destroyed by the encroaching glabellar tumor (peripheral dark gray tissue). x 27.

Glabellar tumor approaching the mucosal surface. The relatively mature type of the tumor accounts for its very slow progress. x 70. (Additional details on next plate)



Chondrosarcoma. Other areas from the glabellar tumor shown on previous plate. A, Calcified cartilage (x 48); B, loose fibromyxoid type (x 75); C, dense, better differentiated cartilage (x 98).



Chondrosarcoma, in a 54 year old man, involved maxilla, posterior nares, orbit, and nasopharynx and eroded into cranial cavity and compressed the pituitary, but did not metastasize. Nasal tumor, removed in 1947, diagnosed osteochondroma; in 1951, chondrosarcoma. Patient died in 1952. Well differentiated cartilage from which the malignant portion seems to arise. Almost all areas of the tumor showed well differentiated chondrosarcoma. x 75. (H. Krogh, Washington)

CHAPTER 23

TONSILS

The **faucial or palatine tonsils** are the most prominent element in Waldeyer's ring which also includes the lateral pharyngeal bands, the pharyngeal granulations, the adenoids, the lymphatic tissue in the fossae of Rosenmüller, the lingual tonsils and those of the eustachian tubes and laryngeal ventricles when they are present. The faucial tonsils lie in the fossa limited anteriorly by the glossopalatine and posteriorly by the pharyngopalatine muscles. They are made up of well organized nodules of lymphatic tissue with prominent germinal centers. The nodules are separated by ten to fifteen deep permanent crypts lined by squamous epithelium. This is a point of differentiation from the pharyngeal tonsil (the adenoids) which has respiratory epithelium lining its crypts. There is usually not the intimate relationship between this epithelium and the underlying lymphatic tissue that there is in the adenoids. The outer portions of the tonsillar mass are defined by a dense fibrous capsule. This capsule is so intimately attached to the muscles of the pharynx that muscle fibers are practically always torn away with it during tonsillectomy. Islands of cartilage and bone are commonly found in the capsule. According to Weller, these are most frequently the result of direct metaplasia of the connective tissue, but they may be inclusions from an abnormally long styloid process. This process develops from the second branchial arch which extends on down to form the hyoid ligament and part of the hyoid bone. Elements of this potentially bony arch are frequently retained in the tonsillar capsule. Whatever their origin, these inclusions have no clinical significance.

The tonsillar tissue differs from lymph nodes in that it has neither a system of sinusoids nor of lymphatics. Normally there is only a delicate connective tissue stroma supporting the cells.

At either pole of the tonsil, particulary at the upper pole, the remaining space in the crypts is occupied by loose areolar tissue which furnishes favorable conditions for the development of peritonsillar infections.

Minear and his co-workers have made a painstaking study of the development of the faucial tonsil, particularly that of the crypts. Originating as epithelial processes growing into the primitive tonsillar masses, they branch and become canalized. Since the canalization begins in the distal portion of the epithelial masses, vesicles are formed that may remain as cysts attached to the permanent crypts by pedicles of epithelium. These attachments are either solid or develop lumens. Normally they disappear shortly after birth. A series of secondary crypts develop later during childhood and there are other possibilities for cysts to originate. The cysts arising from the crypts will be lined by squamous epithelium. Those that are lined by cuboidal or glandular epithelium arise from inclusions in the tonsillar tissue of elements which normally do not empty into the crypts.

A recent book on the tonsil by Parkinson, while written primarily for the surgeon, provides an excellent and beautifully illustrated review of the anatomy, histology, embryology and physiology of the tonsil and allied structures. The author discusses all diseases affecting the tonsils and provides many clinical pictures and photomicrographs of the affected tissues.

Inclusions in the Tonsillar Crypts.—In addition to the accumulations of exudate and debris mentioned under tonsillitis, it is not uncommon to find in the crypts of routinely removed tonsils, large colonies of fungi, including *Actinomyces,* that elicit no particular reaction. In the case of *Actinomyces* the fungus is in a saprophytic phase. It is conceded, however, that under favorable circumstances these colonies are the source of infections not only of the mouth, but also possibly of the rarer primary intestinal form.

At times lime salts are deposited in material in the crypts. This is particularly true when the masses contain fungi. This calcification may accumulate to the point of forming grossly evident stones—TONSILLOLITHS. Weller found calcareous deposits, some only of microscopic size, in eight per cent of 1,000 pairs of tonsils.

The crypts of the tonsils are the harboring place of pathogenic bacteria in carriers of diphtheria and streptococcal and pneumococcal infections.

All lymphatic tissue is in a much more active state in the young, particularly before puberty. With advancing age there is a tendency for the lymphatic tissue to undergo atrophy. In the young, therefore, it is possible to have primary hyperplasia of the tonsillar tissue without an inflammatory component. However, because of the crypts present in all tonsils, secondary infections are possible. Hyperplasia may also occur on the basis of recurrent inflammatory reactions.

In primary hyperplasia the enlargement is due not only to an increase in size of the individual secondary lymph follicles but also to an increase in number. This is not a neoplastic process as is the so-called giant follicular lymphoma of Brill-Symmers that is described under lymph node tumors.

TONSILLITIS

Acute follicular (lacunar) tonsillitis is caused by a direct infection of the tonsillar tissue by bacteria that have gained entrance through a break in the epithelium lining the crypts. Breaks in the epithelium and invasion by exudate are very common.

Clinically the tonsil is enlarged, reddened from congestion, and the crypts are identified by the presence of whitish or yellowish material filling their orifices. This exudate is purulent in character and can be expressed by pressure. Histologically, the crypts are enlarged, there is more or less erosion of the lining epithelium, and exudate, including polymorphonuclear leukocytes, is present in the crypts, in the epithelium, in the superficial portions of the lymphatic tissue, and even in the germinal centers. Abscesses may develop in the tonsillar substance, including the follicles.

Because of the mechanics of the situation, repeated exacerbations of a suppurative process is common. The possible complications are the escape of the infecting organisms into the areolar tissue of the tonsillar fossa, leading to the development of peritonsillar abscess or of a more diffuse cellulitis that may extend to the tissues deep in the neck. When the infection involves the retropharyngeal tissues, the exudate may burrow into the mediastinum. The common offending organisms are *Streptococcus hemolyticus* and *Str. viridans.*

At times the exudate from the crypts forms a pseudomembrane that flows beyond the limits of the crypt orifice and simulates the pseudomembrane of diphtheria. It does not have the fibrin content of the exudate in diphtheria but is more yellowish in color and on removal does not uncover a raw, bleeding surface. Rarely is the faucial tonsil alone involved, but there will be a certain amount of reaction also in the lingual and pharyngeal lymphatic masses.

Acute ulcerative tonsillitis results from the erosion of an intratonsillar or a peritonsillar abscess. It is also a feature in some of the specific infections such as influenza and scarlet fever. In the last instance it is the result of local streptococcal infection. Most specific necrotizing processes result from infection by the organisms of Vincent's angina. The ulcerating gangrenous reaction is a complication of agranulocytosis and of other blood diseases.

Chronic tonsillitis is very common, especially in adults, and results from repeated acute inflammations. With the normal regression in the amount of lymphatic tissue incident to aging, there is an increase in the fibrous stroma. This at first is an accentuation of the normal tonsillar trabeculae. In addition, there is focal scarring as residuum of former suppurative lesions. The tonsils, therefore, become smaller, more irregular in contour, and crypts that are not obliterated may still be filled with exudate. This exudate is usually more caseous than purulent because it is made up chiefly of keratinous debris, saprophytic fungi, and bacteria. There may also be cholesterol crystals and occasionally calcium deposits. The masses are usually larger in the crypts that open into the supratonsillar fossa and those that are covered by the plica tonsillaris.

Chronic tonsillitis is more specifically a clinical than a pathologic entity. It usually results from repeated exacerbations of infection. Its extent may not always be demonstrable histologically. An exaggerated physiologic atrophy with a certain amount of replacement fibrosis might resemble histologically the tonsil that is the seat of the chronic inflammatory process.

The tonsils the seat of these accumulations have been regarded as focal-infection points for systemic diseases. There is a question as to whether this is or is not strictly true, but there is a suggestive relationship between the incidence of streptococcal infections of the tonsils and rheumatic fever. It is assumed by many that rheumatic fever is a hyperergic reaction to streptococcus. These chronically infected tonsils may be the seat of acute exacerbations even in adults. The tonsillar masses share in general inflammatory reactions with the pharyngeal mucosa. It is the lymphatic-tissue accumulations and the presence of the crypts that make their reaction a more obvious and more prominent feature clinically.

All the elements of the tonsillar ring of Waldeyer show similar reactions to age and local inflammatory processes, but because of locations there are clinical features specific for each element. These can be listed categorically as: Tornwaldt's disease associated with the pharyngeal tonsil; middle ear infections associated with the lymphatic tissue about the eustachian orifices; peritonsillar abscess (quinsy) associated with the faucial tonsils; abscess or phlegmonous inflammation of the tongue associated with the lingual tonsils.

Peritonsillar abscess (quinsy) is most common in young adults and results from infection of the peritonsillar capsule and the areolar tissue in the supratonsillar fossa. As a result there is a local accumulation of pus, with edema involving the soft palate. The pus tends to dissect downward and backward, and when the deep structures of the neck are involved the pharyngomaxillary abscess results. It may extend down to the mediastinum or involve the great vessels of the neck.

ATROPHIC LESIONS

Atrophy. — Kelemen would distinguish between the "normal" atrophy of the tonsil in advanced years and an inflammatory fibrosing process. In the aging process there is a simple reduction in cellular content of the tonsil without fibrosis. The connective tissue stroma of the tonsil becomes only relatively prominent. By this means the tonsil may be reduced to a single everted crypt with little or no remaining lymphatic tissue element.

Another type of fibrous atrophy of the tonsils is produced by attempts at removal by direct irradiation or by electrocauterization. Irradiation causes a marked reduction of the lymphatic tissue element, particularly of the germinal centers, and a considerable increase in the trabecular fibrous stroma. The epithelium usually shows atrophy and dyskeratotic changes.

Electrocoagulation also reduces the lymphatic tissue and destroys the germinal centers. The chief difference in the two lesions is the more irregular and scar-like masses of connective tissue in the cauterized tonsil and the absence of changes in the epithelium. When the scarring involves the capsule a greater amount of the striped muscle than usual will be torn away during tonsillectomy.

GRANULOMATOUS INFLAMMATIONS

Tuberculosis of the tonsils occurs most commonly in a clinically obvious form, but there is an appreciable incidence of latent and clinically occult infection. Meyerson states that the tonsils are more likely to become infected than any other part of the upper respiratory tract, usually as a complication of advanced pulmonary disease. Under this circumstance the infection is most frequently a direct one from infected sputum, but transmission by the blood and lymph streams is at least possible. Clinically, it appears as a localized, confluent, ulcerating lesion that tends to involve the neighboring tissues as well, or as a deeper, more generalized miliary process—indicative of a blood-borne infection.

The occult type of infection is more common in children and represents in some instances, at least, a primary infection. In the days before our present effective dairy hygiene the bovine type of bacillus was not an uncommon offender. The incidence of the latent infection seems to be decreasing and is probably less than one per cent in the white population in this country. Tuberculosis of the cervical lymph nodes—the clinical scrofula—results from tonsillar infection.

Syphilis.—The primary lesion has been reported on the tonsil and condyloma occasionally develops in the fauces, but the pharynx, fauces and tonsil are more common sites of the secondary mucous patch.

Sarcoid is not uncommon in the faucial tonsils. It is difficult to differentiate from tuberculosis because the tubercles in the latter are frequently of the sarcoid type.

TUMORS OF TONSILS

Cysts.—A rare form of cyst is the result of inclusion of embryonal elements with the production of a cystadenoma. The commonest, however, are the cysts that result from inclusion of surface squamous epithelium as mentioned earlier. These will contain keratinous debris and cholesterol. The DERMOID CYST occasionally appears in the pharyngeal wall.

One of the commonest tumors of the faucial tonsil is the simple **papilloma.** It is a benign lesion, although one showing leukoplakic dyskeratosis is included in the plates. An interesting example of a diffuse papillomatosis is also illustrated. The patient was an 11-year-old boy who had been in good health except for enlarged tonsils. A diffuse, soft, frond-like lesion covered one tonsil and the posterior pillar, extended onto the glossoepiglottic fold and well down into the pyriform fossa. This altered mucosa was stripped off, but the operation was too recent to judge results.

Fibroma.—There is not the variation in sex incidence for fibroma in this location that there is in the nasopharynx, but it is more frequently seen in the young. It is embedded in the substance of the tonsil or more usually it is pedunculated. It does not have the vascularity of the nasopharyngeal fibroma. Histologically, it is made up of entwining bundles of spindle cells with a varying content of collagen fibers. It is a benign tumor.

Vascular tumors, more commonly the simple HEMANGIOMA and LYMPHANGIOMA occur particularly in the subcapsular tissue. These are usually more hamartomatous than neoplastic, that is, exaggerations of vascular elements normally present.

Malignant tumors.—The tonsils may participate in the systemic neoplastic processes, the malignant lymphomas. Reticulum cell sarcoma does occur as a primary tumor in the tonsil, but not so frequently as it does in lymph nodes where reticuloendothelial elements are more abundant. Otherwise the commonest malignant tumor of the tonsillar tissue is carcinoma. It is frequently undifferentiated, especially that of the pharyngeal area, and is sometimes, therefore, difficult to distinguish from reticulum cell sarcoma.

Carcinoma of the faucial tonsil is much more common in the male and in the older age groups than is nasopharyngeal carcinoma. It can develop on the basis of leukoplakia. It is most commonly of squamous cell type because of the epidermoid type of epithelium covering these tonsils. Schall classified as squamous cell carcinomas approximately ninety-five per cent of 154 cases that he studied.

Not infrequently squamous cell carcinoma of the fauces develops as a superficially spreading lesion instead of the more localized and penetrating one. It is very deceiving clinically. In spite of its leukoplakic character histologically, it is not so grossly. It begins as a "sore throat," with ulcerations and bleeding refractory to treatment. It is only by biopsy that its true nature is revealed. In the meantime it is likely to have spread from the tonsillar area to the mouth and hypopharynx. It is very sensitive to irradiation therapy, fortunately, because surgical eradication is scarcely practicable. It does not metastasize as early as the more infiltrating carcinomas of the mouth and pharynx.

Metastatic tumors in the tonsils are very rare.

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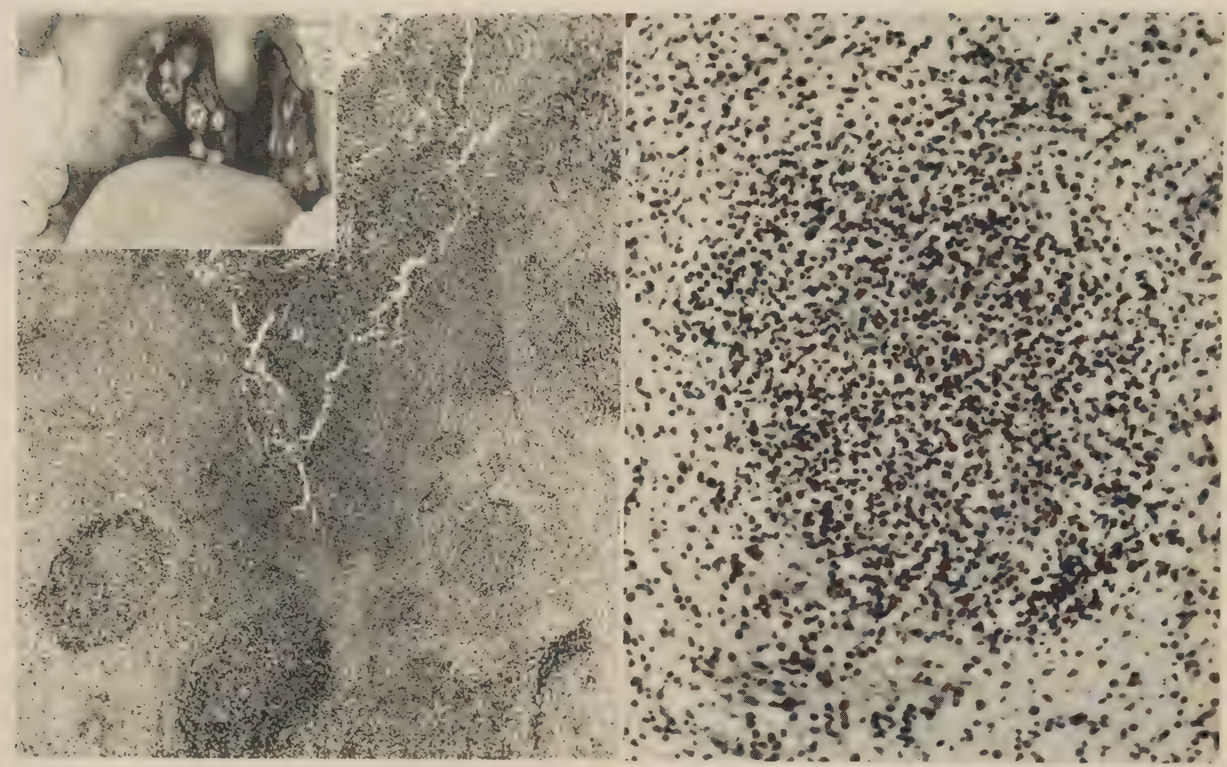
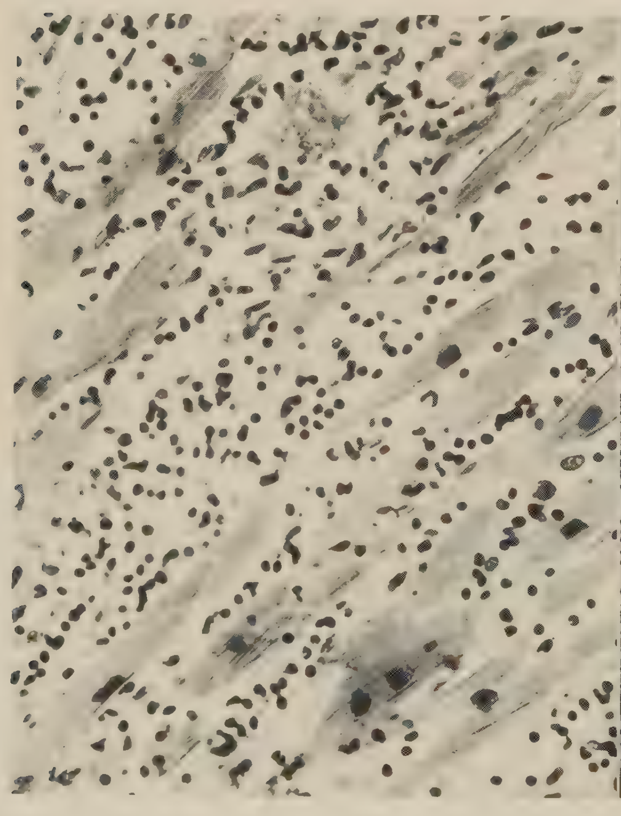
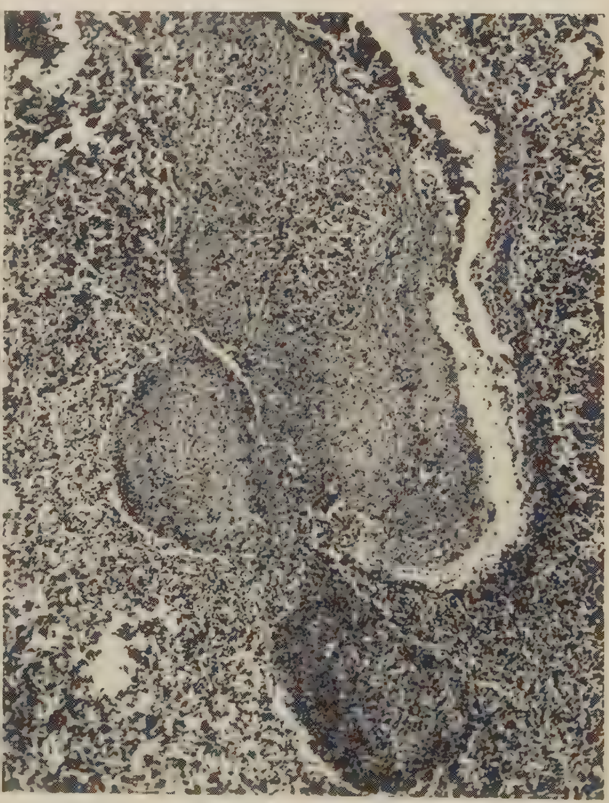


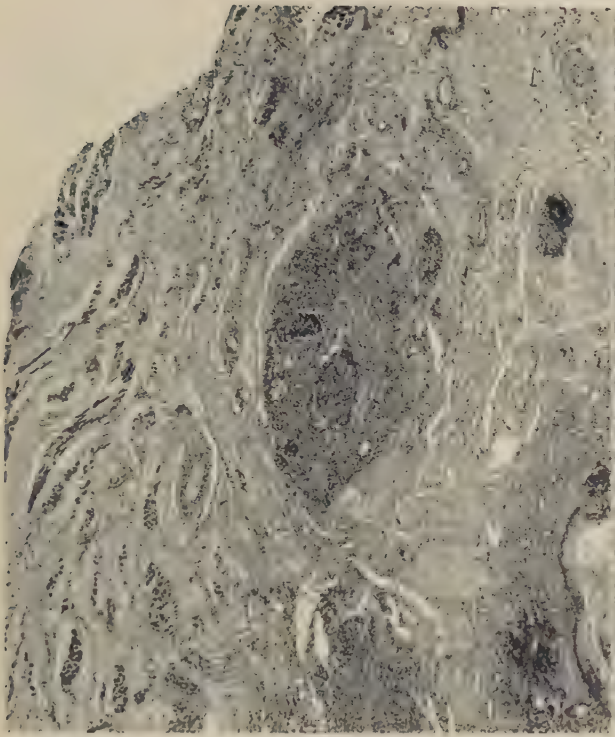
Acute tonsillitis with abscess formation. The clinical picture of the follicular type, the crypts filled with yellowish debris that mushrooms over the surrounding surface, is seen in the insert. An abscess developing in a crypt involves neighboring follicles. x 45, x 185.



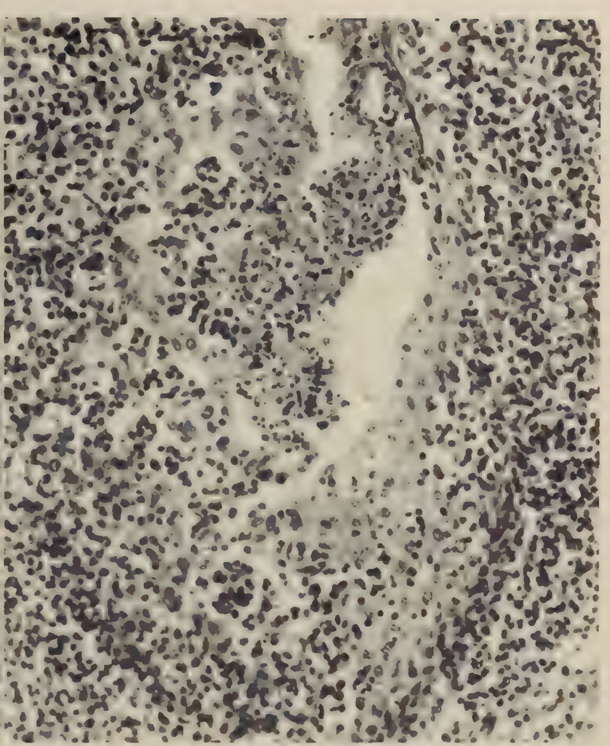
Acute myocarditis complicating acute tonsillitis; possibly streptococcal. x 435.



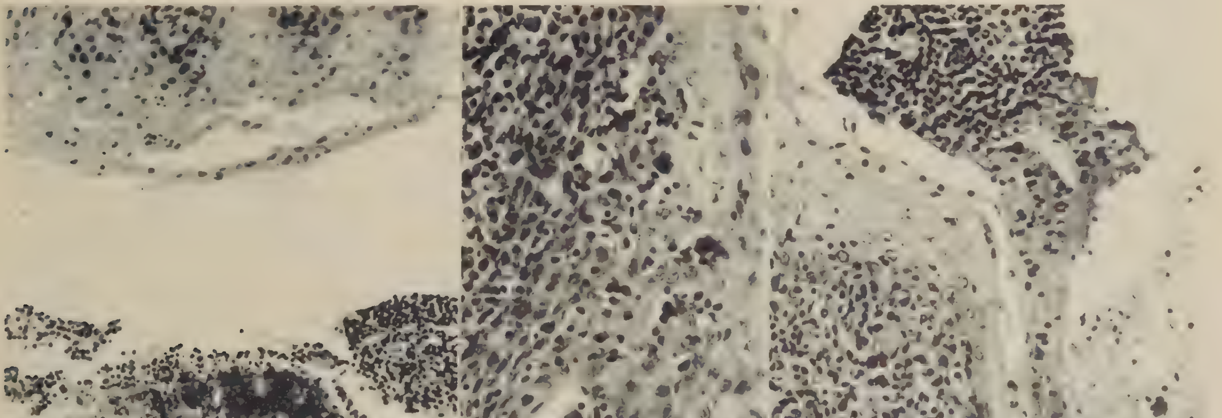
Diphtheria. The crypt is filled with false membrane intimately applied to the ulcerated surface. x 175.



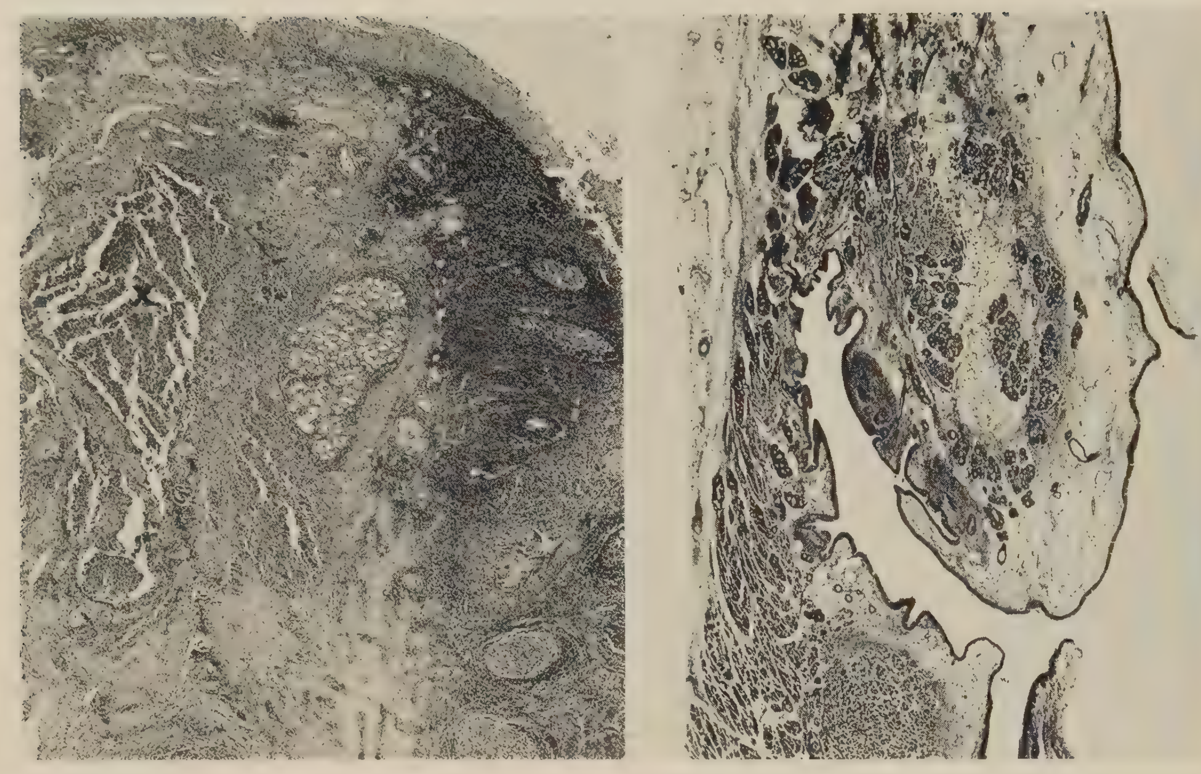
Phlegmonous inflammation of tonsillar bed associated with streptococcal cellulitis of neck. Crypts are filled with purulent exudate; vessels of the fibrous capsule are congested. x 20.



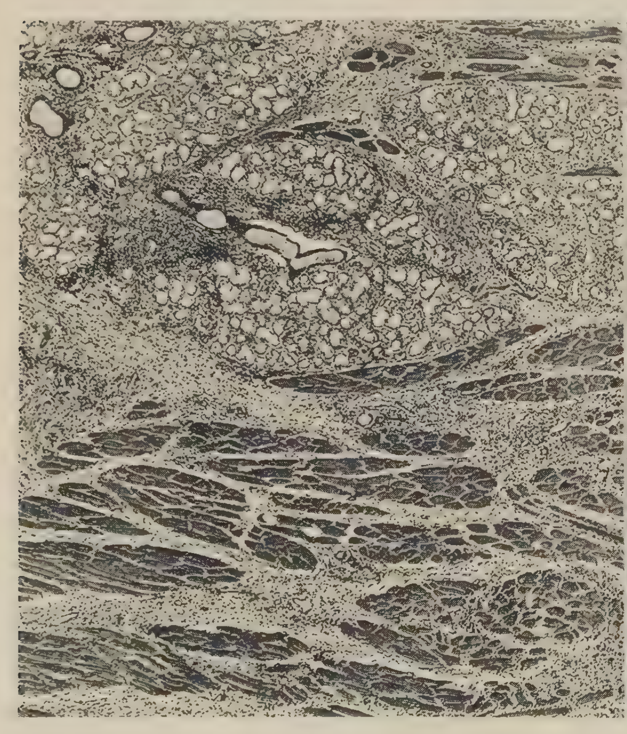
Subacute tonsillitis. Crypt with ulcerated lining and exudate of polymorphonuclear leukocytes and plasma cells. x 185.



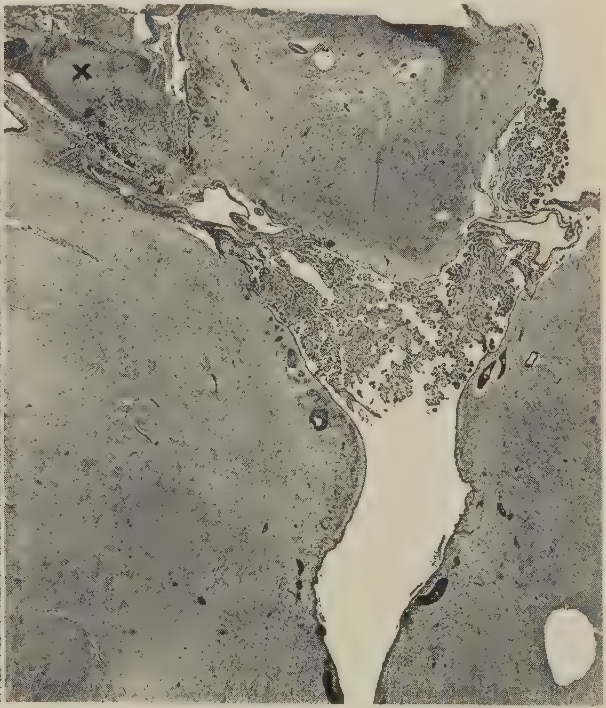
Additional details from the case at right, above: A. Colony of bacteria and cellular exudate with conspicuous plasma cells on surface of crypt. x 125. B. Subepithelial and intraepithelial nests of plasma cells. x 205. C. This crypt is plugged with exudate that expands onto the surface. x 185.



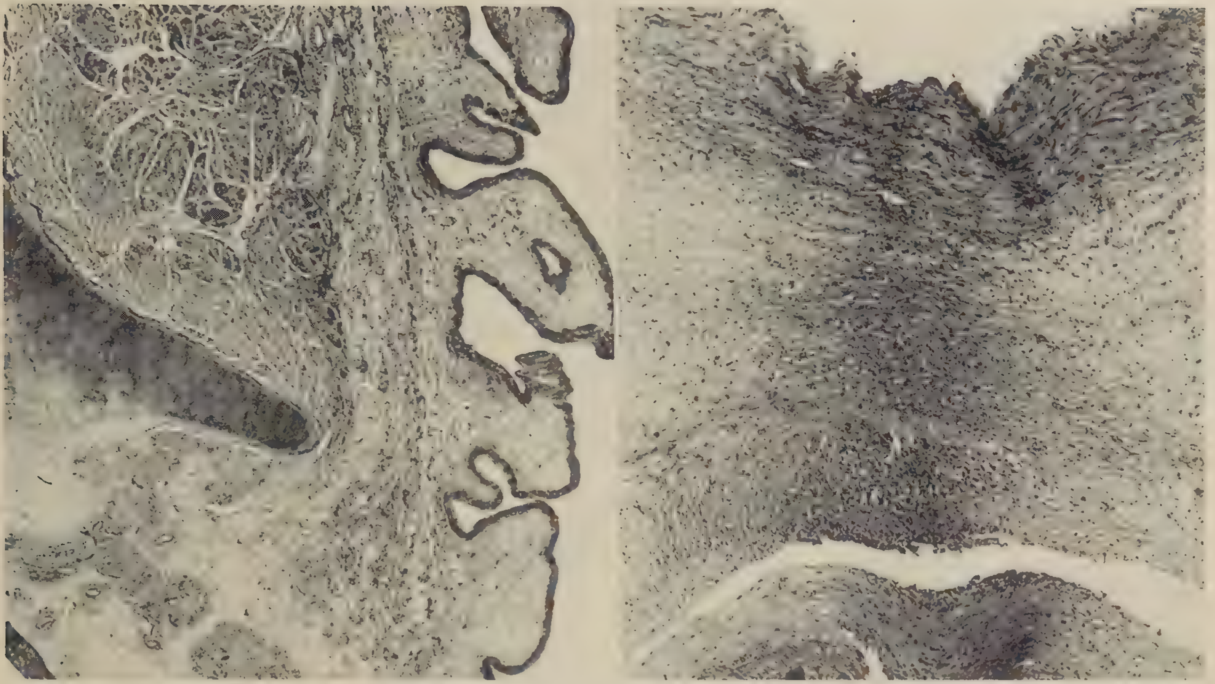
Peritonsillar abscess (quinsy) in a 22 year old man, who died from edema of the glottis during operation. Peritonsillar tissue is heavily infiltrated with purulent exudate, including several concentrations forming clinical abscesses. x 24. Section of larynx to show edema of the false cord. Small mass of lymphoid tissue (laryngeal tonsil) in wall of ventricle. x 9.



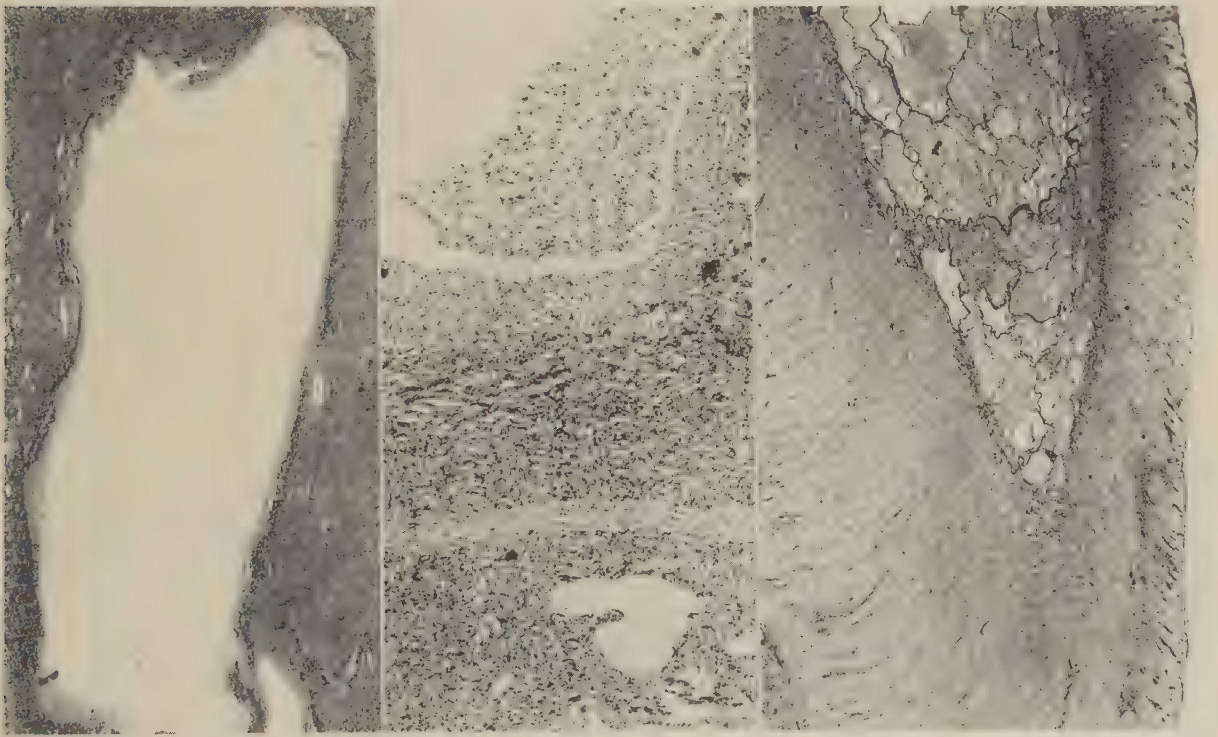
Suppurative inflammation of pharyngeal wall including muscle layer (from case above). Dense polymorphonuclear cellular infiltration around glands and widely separating muscle bundles. x 39.



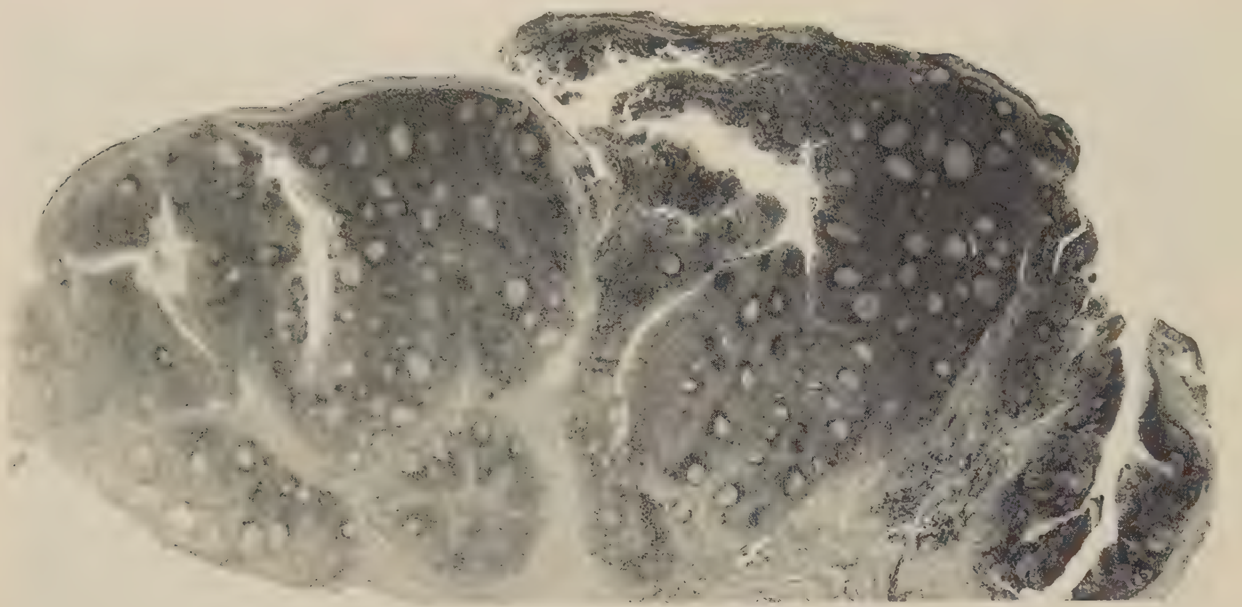
Brain abscess (x) which ruptured into lateral ventricle (x 7) was one of several that caused cerebral symptoms and death of a 25 year old man, 1 month after incision of a peritonsillar abscess.



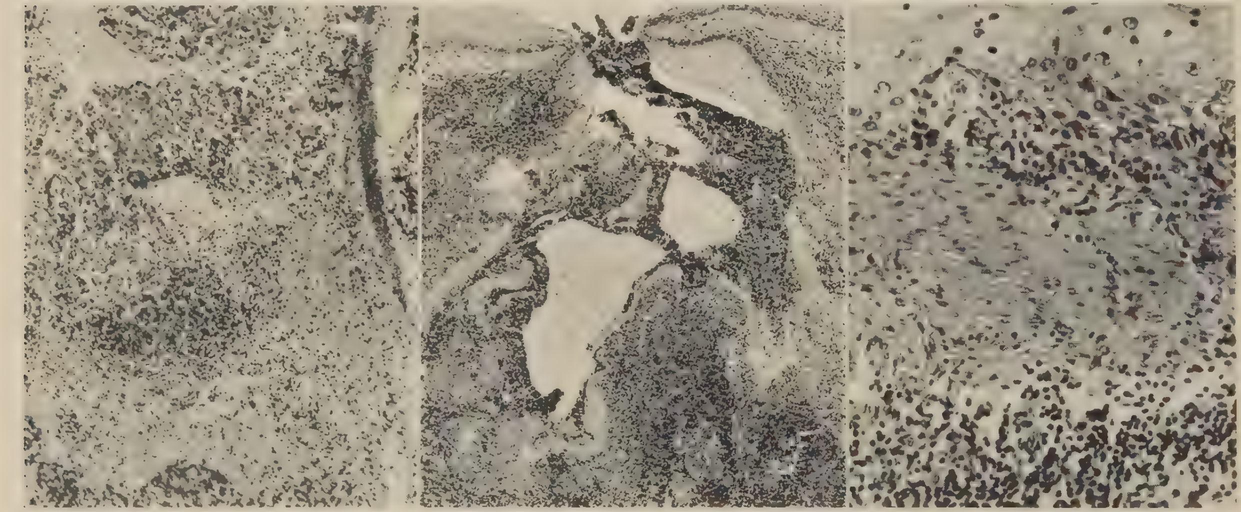
Peritonsillar abscess in an 18 year old man. The abscess was incised November 13, 5 days after onset of symptoms. Peritonsillar swelling recurred November 29; ligation of external carotid artery was performed December 13 for severe hemorrhage, and tracheotomy, December 16. The patient died the following day. At left, polypoid supraglottic edema, necessitating tracheotomy. x 10. At right, necrosis extending through wall of internal carotid artery. Thrombus above this point. x 62.



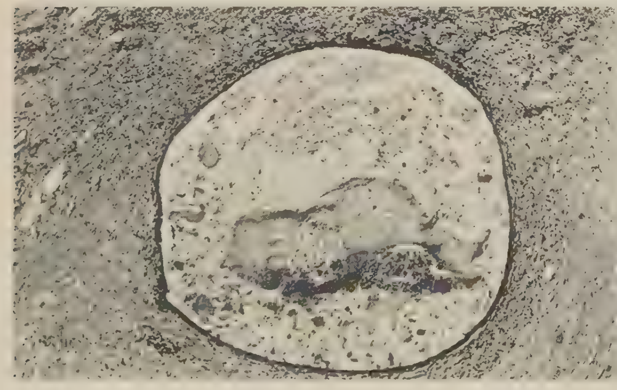
A. Lung abscess (x 7) and **B,** pyogenic membrane lining abscess (x 50), resulting from peritonsillar abscess which had been present for a month in a 20 year old man. Multiple pulmonary abscesses and edema were found at autopsy 3 weeks after incision of the abscess and tonsillectomy. **C. Encapsulated empyema,** chest wall, from patient with multiple brain abscesses, illustrated on preceding plate. x 10.



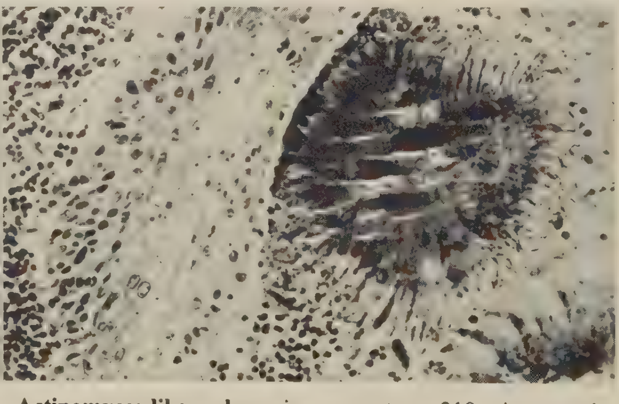
Enlarged tonsil, showing follicular hyperplasia, removed from a 20 year old man 2 weeks after acute tonsillitis. Ulceration at surface of some crypts, many of which contain considerable exudate. Thickened fibrous trabeculae extend up from capsule. x 7.



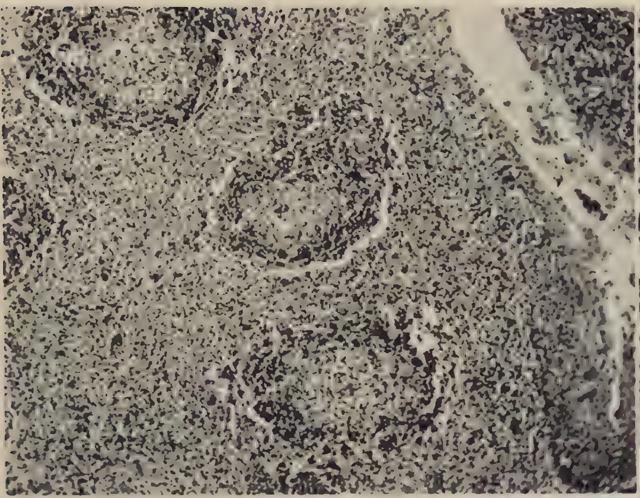
Histologic details in chronic tonsillitis: A. Focal stromal hemorrhage with surrounding edema. x 75. B. Ulcerated crypt with plugged orifice filed with serum, fibrin, and cellular exudate. x 48. C. Area of subepithelial fibrosis. x 185.

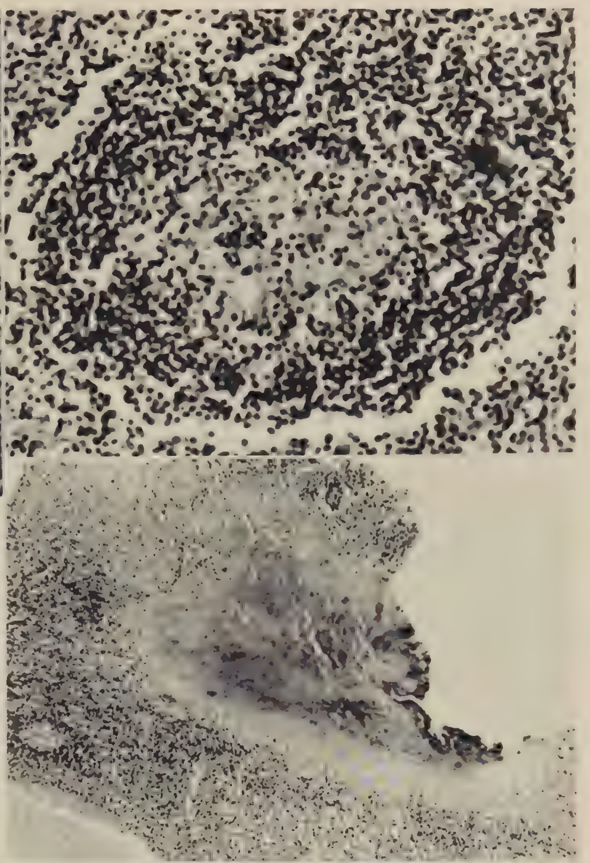


Retention "cyst" that developed in crypt with an occluded orifice in a fibrotic tonsil. x 215. (H. P. Mosher, Boston).

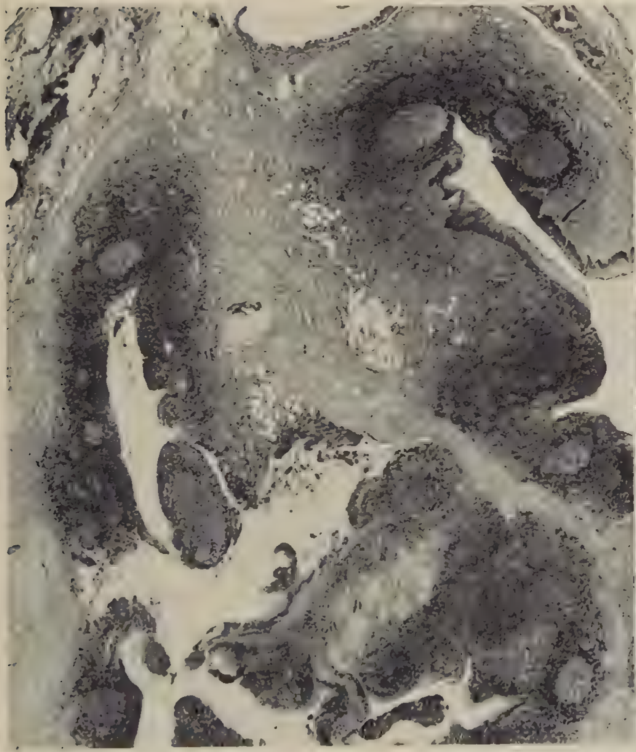


Actinomyces-like colony in a crypt. x 210. Apparently innocuous colonies of bacteria and fungi are often present in crypts (botryomycosis; staphylococcic actinophytosis).

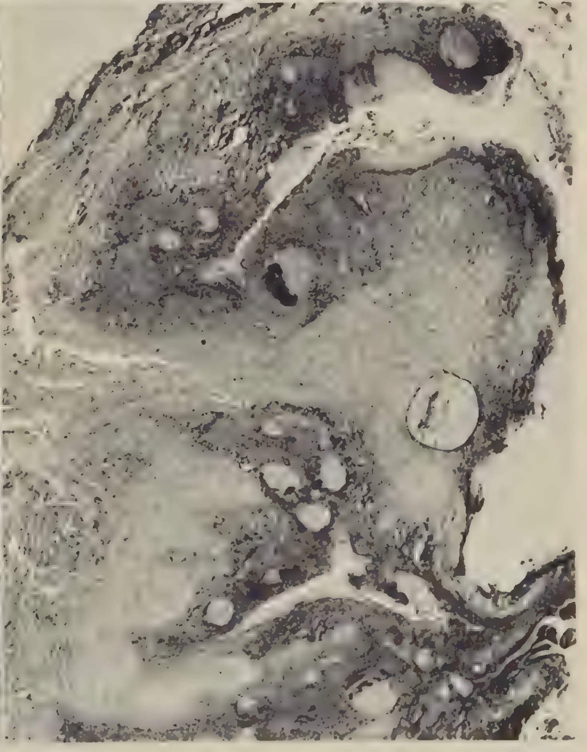




Irradiation effects. A and B. Atrophy of lymphatic tissue is masked by proliferation of atypical mononuclear cells resembling reticulum cells or lymphoblasts, in tonsil from patient who sustained mid-lethal irradiation injury from an A-bomb explosion. C. Extensive necrosis from "x-ray removal" of tonsil.



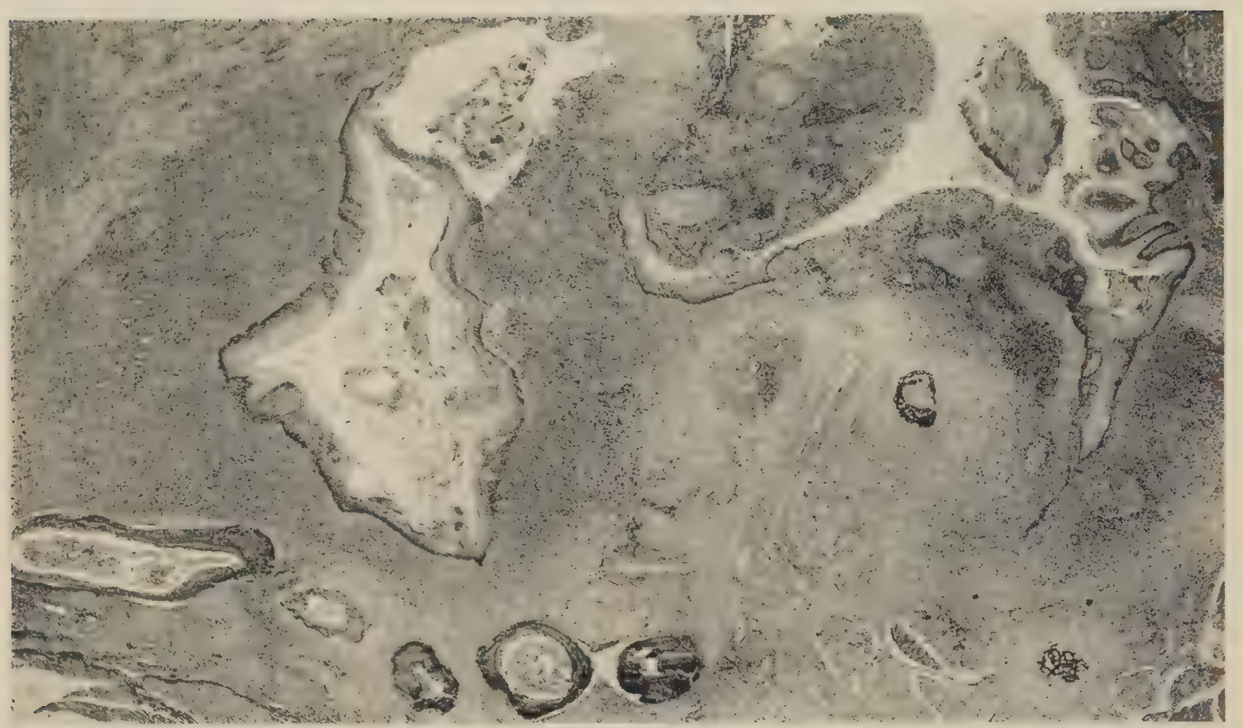
Intense scarring of tonsil removed from a 68 year old man after 3 months of electrocoagulation therapy. Bone and cartilage in capsule are incidental. x 10. (S. S. Hall, Clarksburg, W. Va.).



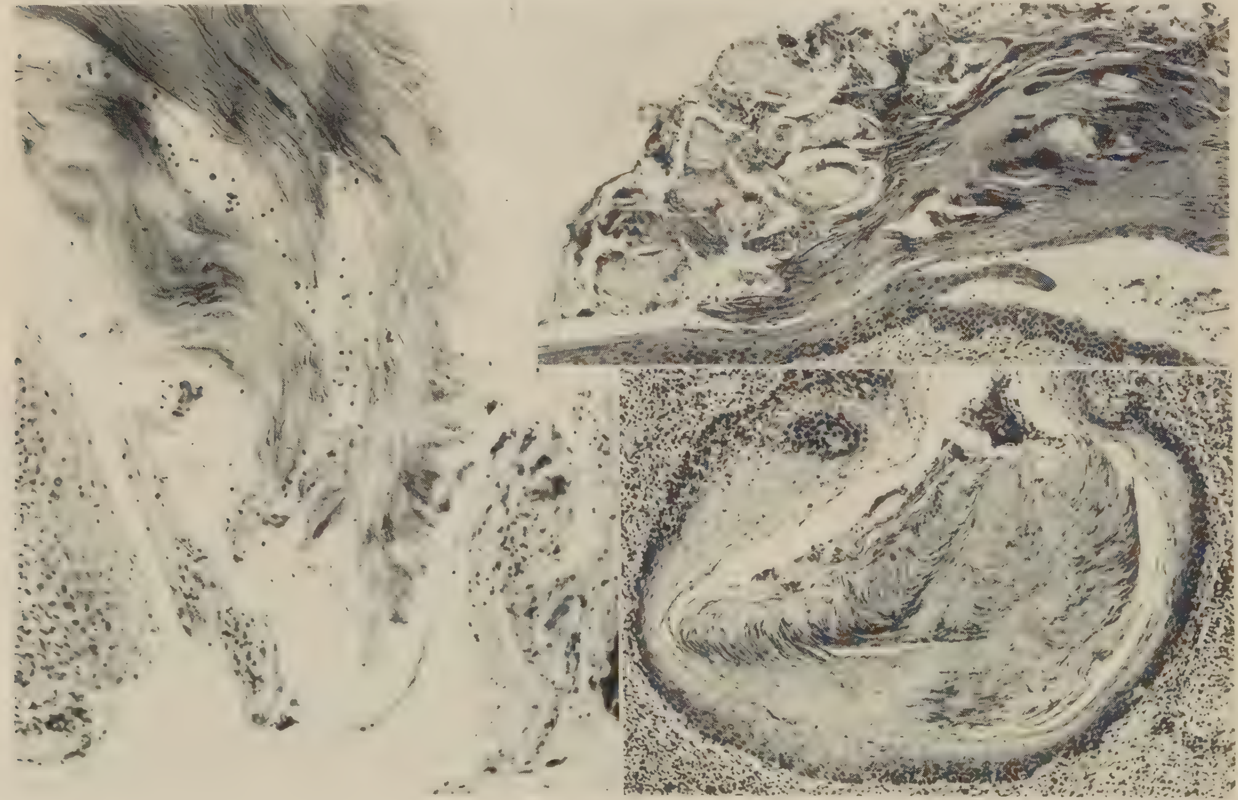
Fibrosis from prolonged inflammation of tonsil, from a 75 year old man. Massive scarring and great reduction in lymphatic tissue. x 12.

HYPERKERATOSIS, TONSIL

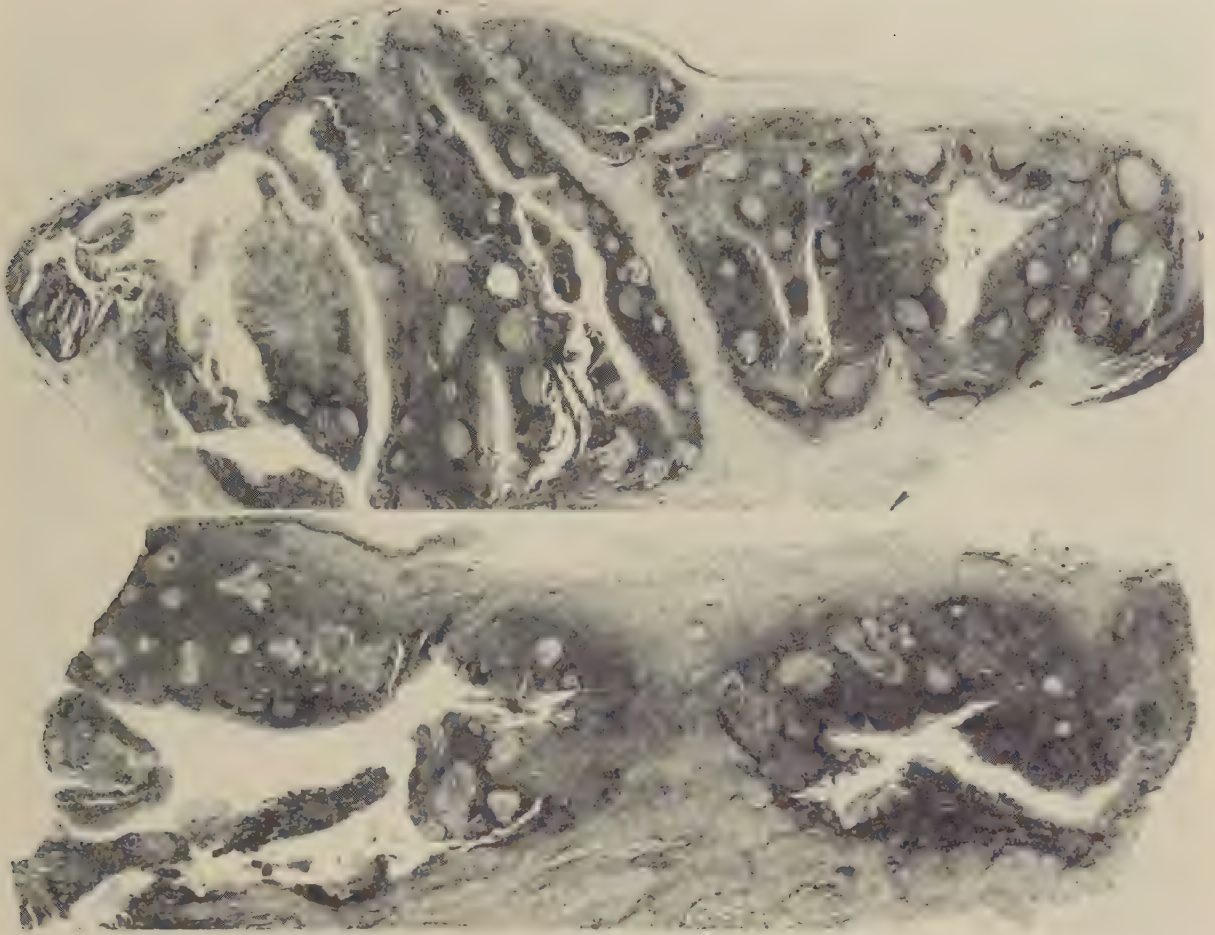
CARTILAGE AND BONE



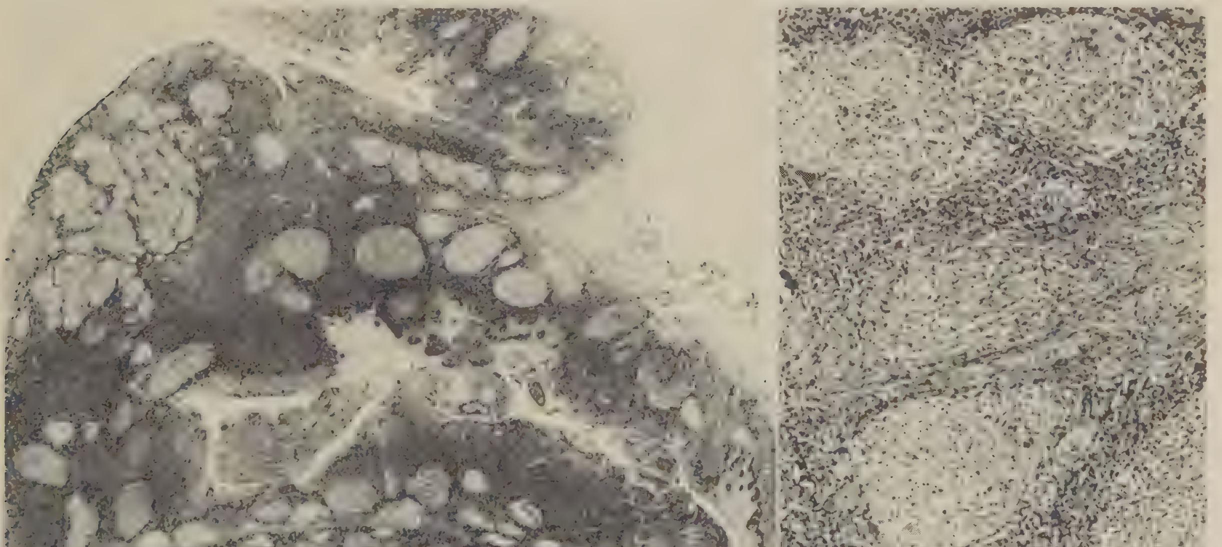
Hyperkeratosis, tonsil, from a 42 year old man. Distended crypt filled with masses of keratin. Scattered areas of fibrosis throughout. Note cartilage and bone, found in 10 per cent of tonsillectomy cases and associated with fibrosis, usually due to chronic infection. x 2½. Mild pharyngitis for several months. Firm tapioca-like particles in crypts of faucial and lingual tonsils and scattered over pharynx and edge of epiglottis were adherent, but were removed without bleeding.



A. and **B.** Within the masses of keratin are bacteria and fungi, which are commonly found with hyperkeratosis. x 125, x 75. **C.** Cross section of crypt packed with compressed keratin. x 75.



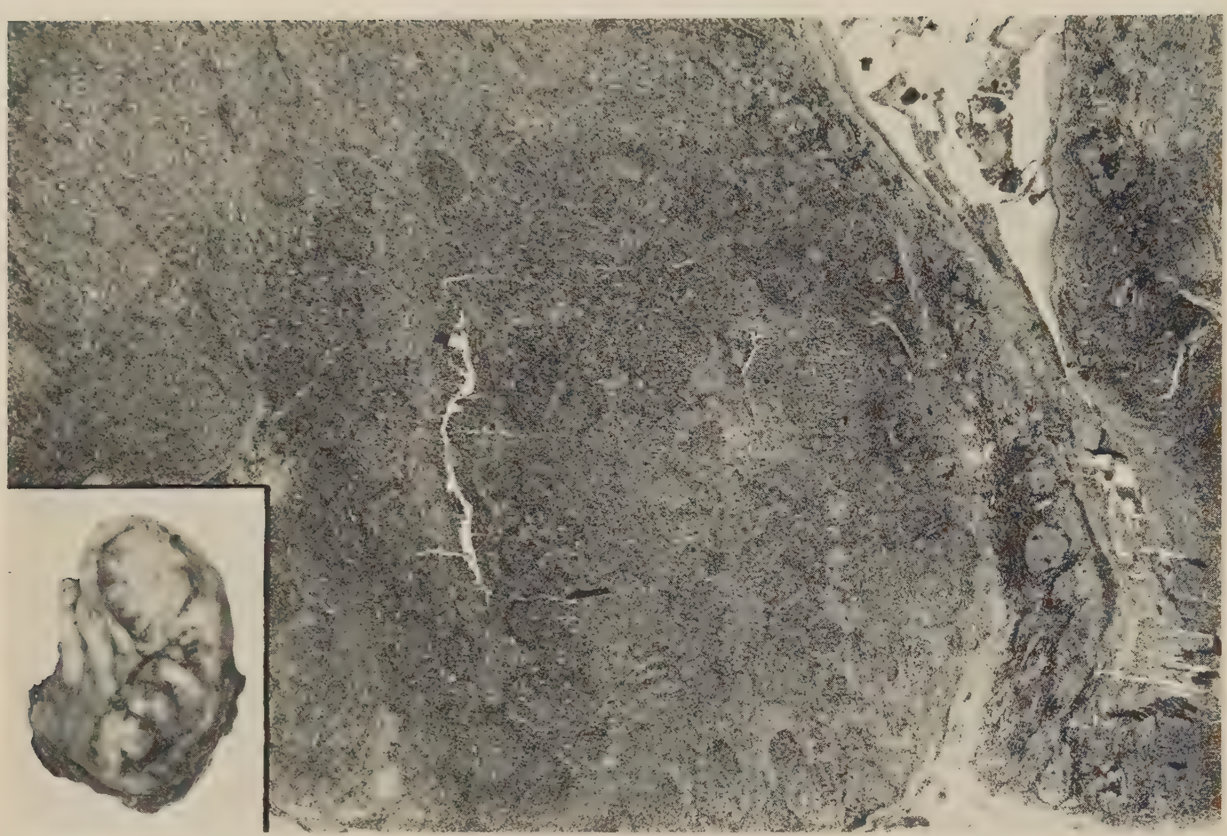
Tuberculosis, tonsil. Tubercles (pale, discrete foci barely distinguished, above; large, prominent and numerous, below) may have central areas of caseation necrosis, are usually more regular in shape and distribution, and, if conglomerate, larger than follicles. At this low magnification such differentiation is especially difficult in section of tonsil, at top, from a 26 year old woman with a diagnosis of chronic follicular tonsillitis.



Sarcoidosis, tonsil, from a 24 year old Negro with x-ray diagnosis of sarcoidosis of lungs. A. Tubercles and follicles. x 14. B. Four sarcoid tubercles made up of epithelioid cells and an occasional giant cell can be distinguished from segment of follicle in the lower right hand corner. x 75.

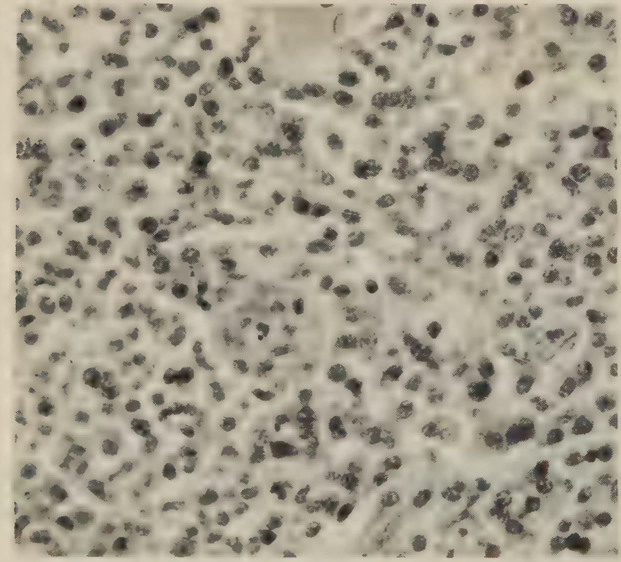
SYPHILIS, TONSIL

PRIMARY AND SECONDARY LESIONS

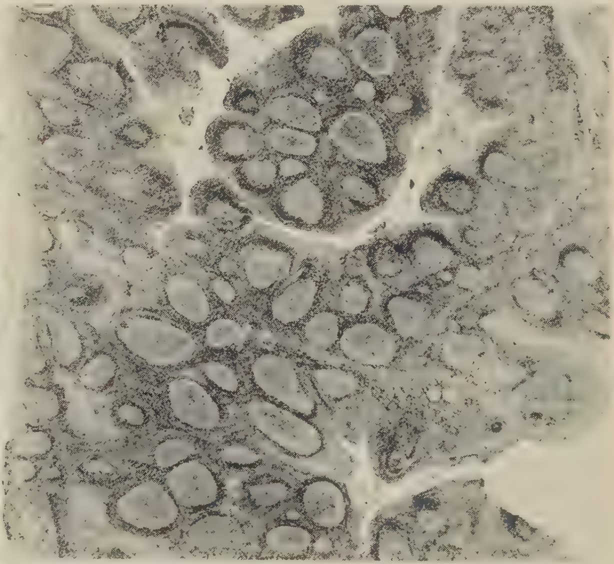


Chancre, tonsil *(inset).* A 23 year old man with sore throat and left cervical lymphadenopathy. Two dark field examinations positive for *Treponema pallidum.* Kahn, then Wassermann reaction became positive; generalized maculopapular rash subsequently developed.

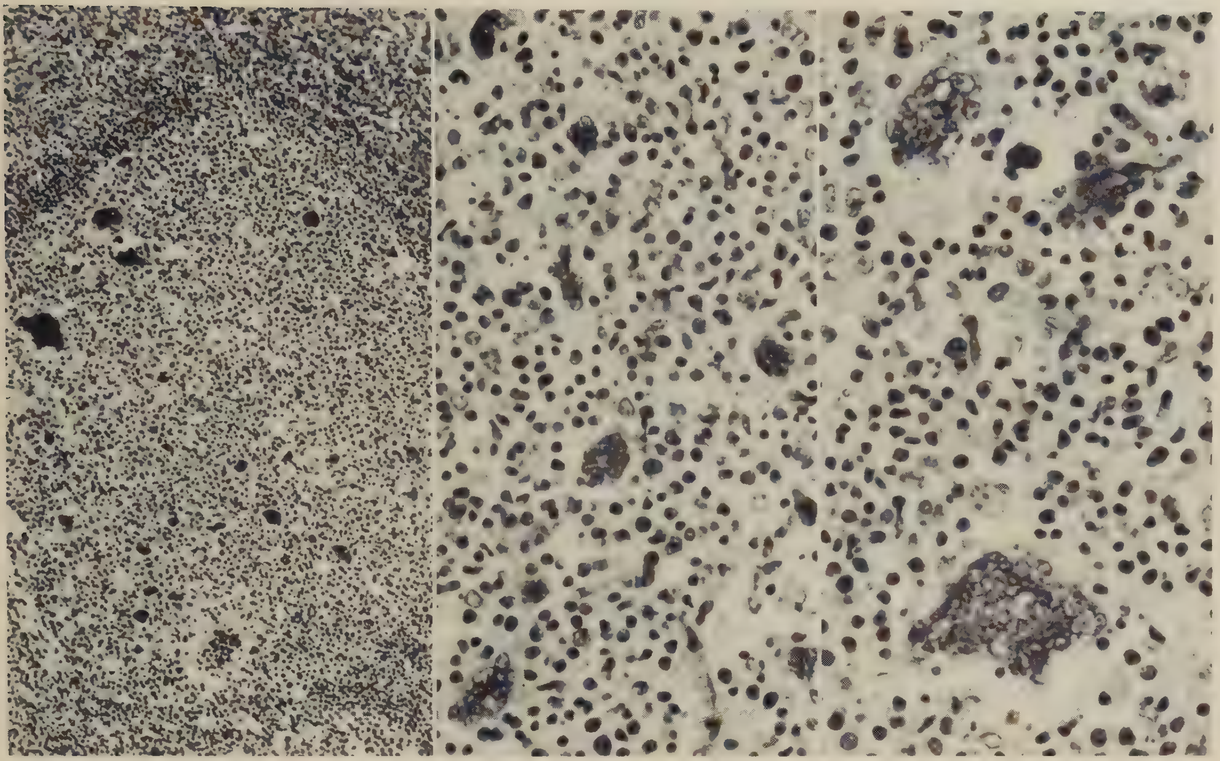
Secondary syphilis, tonsil. A 34 year old man with persistent sore throat and hypertrophied tonsils. Generalized macular eruption followed bilateral tonsillectomy. Diffuse obliteration of normal follicular structure in greatly enlarged tonsil. x16. Similar opposite tonsil also had superficial plaque considered the primary lesion.



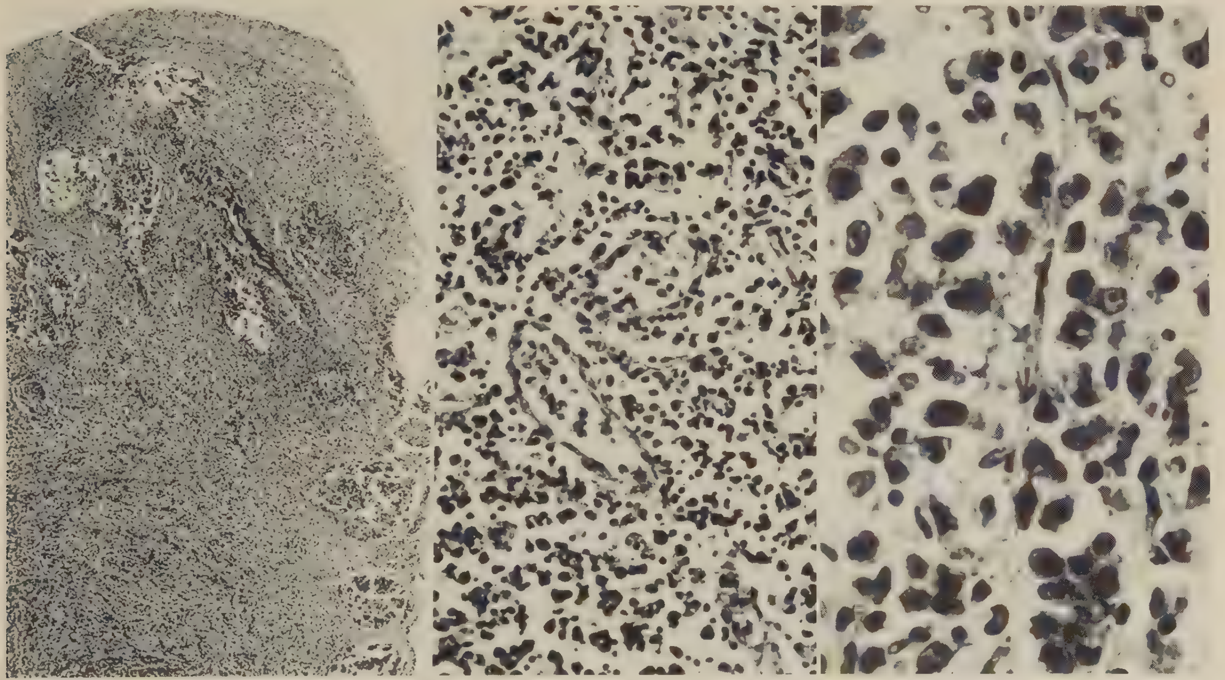
Histopathology of the secondary lesion. Proliferating capillaries with hyperplastic endothelial cells surrounded by dense cellular exudate, chiefly plasma cells with some lymphocytes and macrophages. x395.



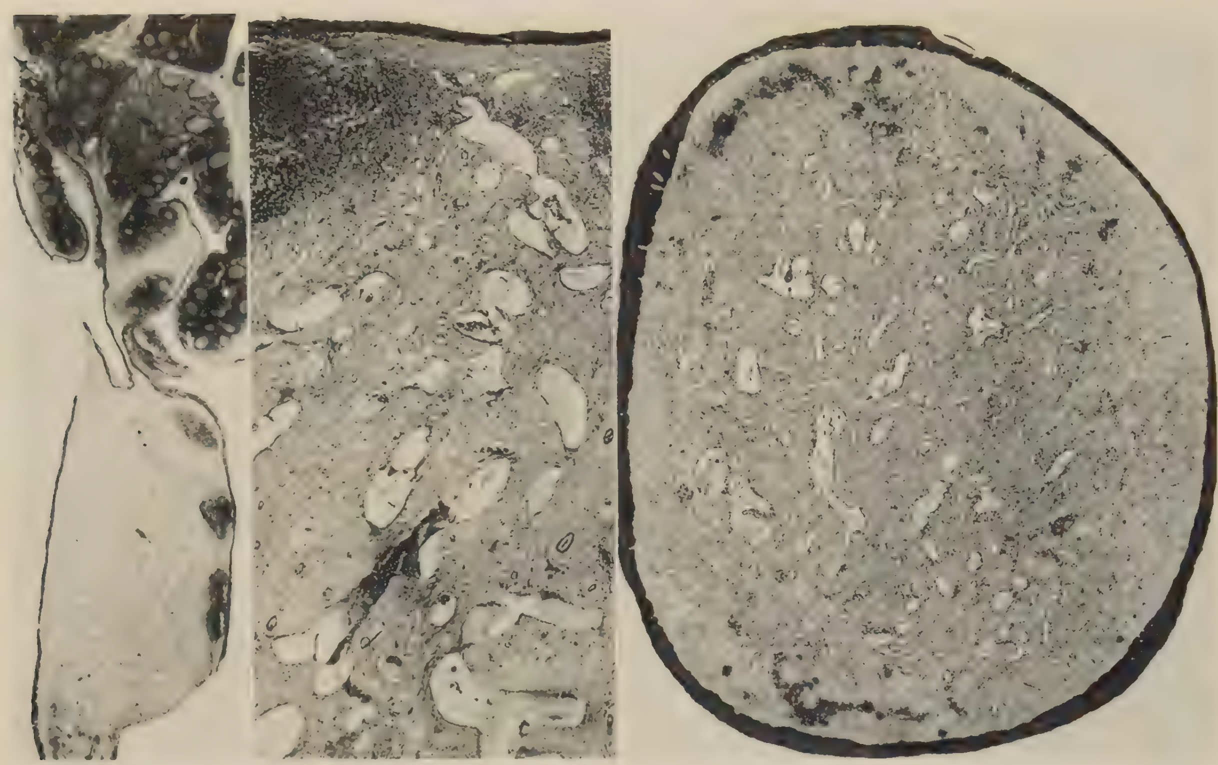
Chronic hyperplastic tonsillitis, not luetic. Numerous well defined follicles with prominent germinal centers, in contrast to the diffusely obscured pattern of the lymphoid tissue illustrated *above.* x11.



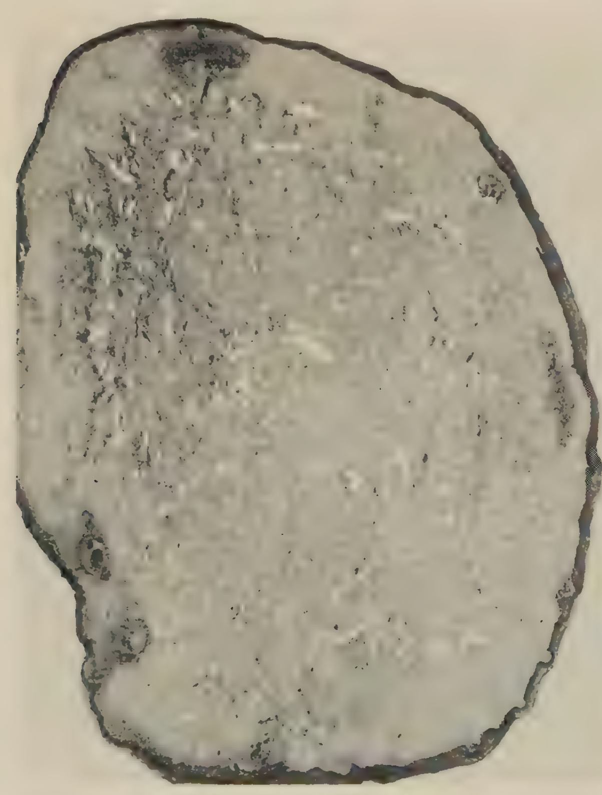
Measles. Atypical cells, usually multinucleated giant cells, appear in the germinal centers of lymphatic tissue in various parts of the body including the tonsils, even before the rash. These distinctive giant cells (Warthin–Finkeldey cells) are shown in increasing magnification; a germinal center, at left, for purposes of orientation. x 75, x 325, x 400.



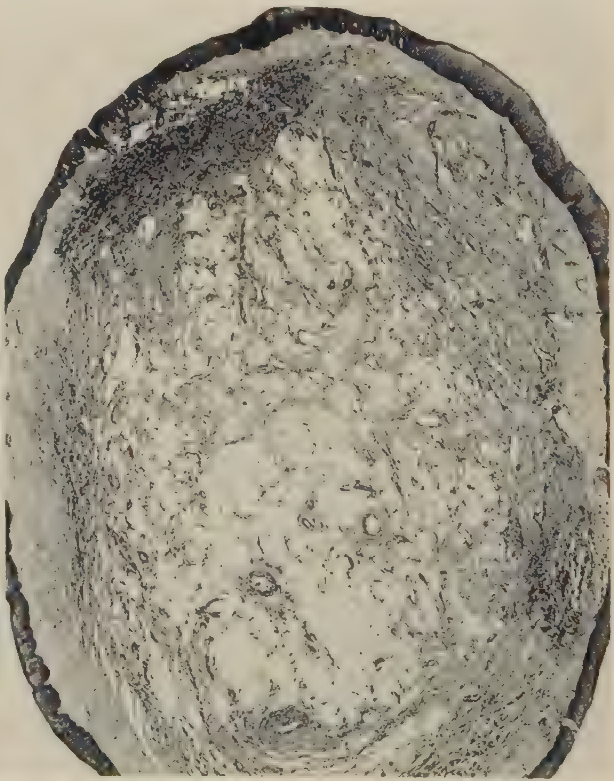
Infectious mononucleosis. The reaction in lymphatic tissue is diffuse, blurring the normal architecture. At left, a few peripheral follicles remain. x 24. At center, intravascular and extravascular abnormal lymphocytes and hyperplastic reticuloendothelial cells. x 275. At right, the large atypical lymphocytes, several in mitosis, are the Downey cells seen in the peripheral blood. x 605.



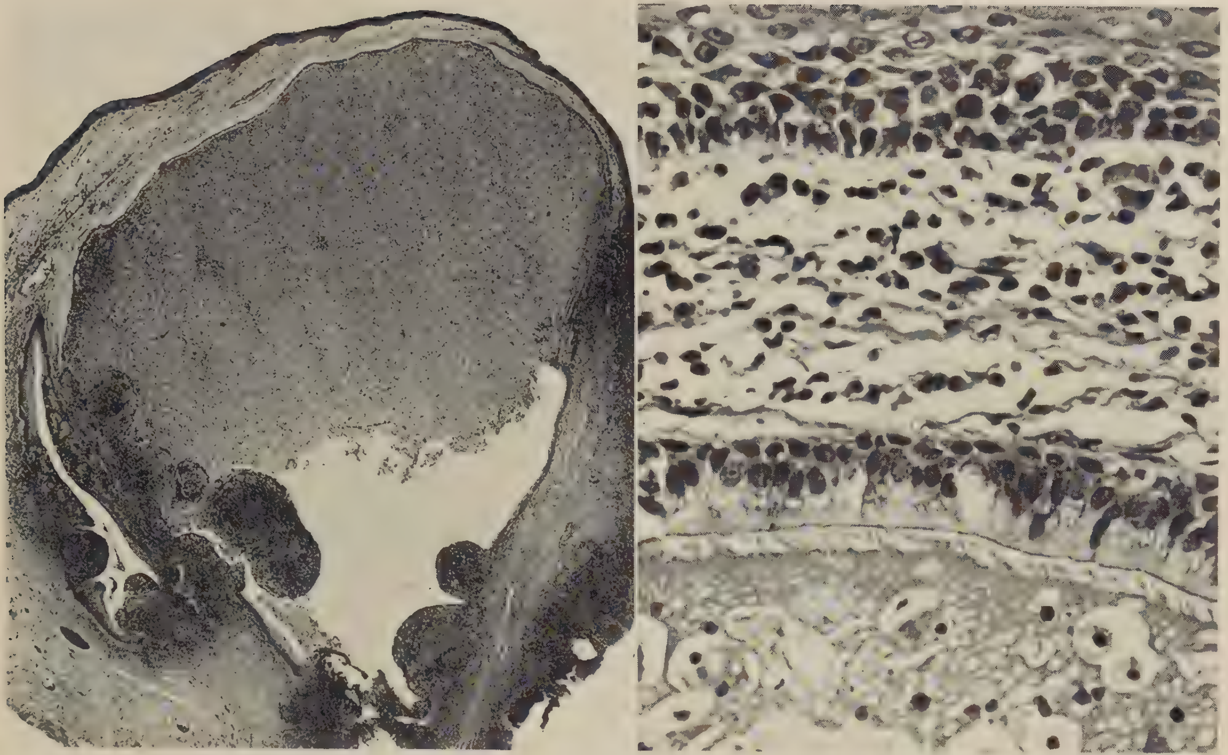
Lymphangiectatic fibrous polyps. Left, from tonsil of a young man. In a stroma of cellular and moderately edematous fibrous tissue are many dilated lymph vessels which show no evidence of proliferation. x 5, x 28. Right, a similar polyp with a more prominent fibrous component. x 15. Submitting diagnosis was lymphangioma, but it is not a neoplasm.



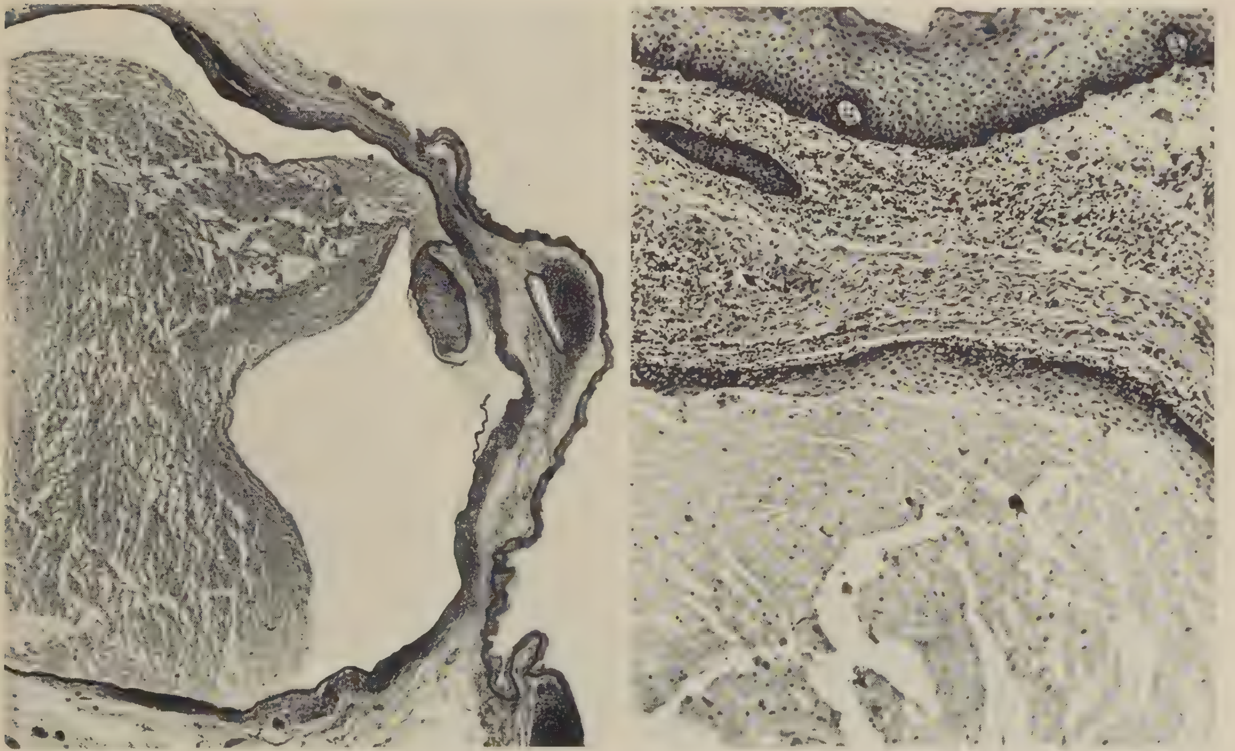
Fibrous polyp. More advanced fibrosis in a polyp with thick-walled blood vessels as well as lymph vessels, neither being neoplasic. Note residual lymphatic tissue. x 18.



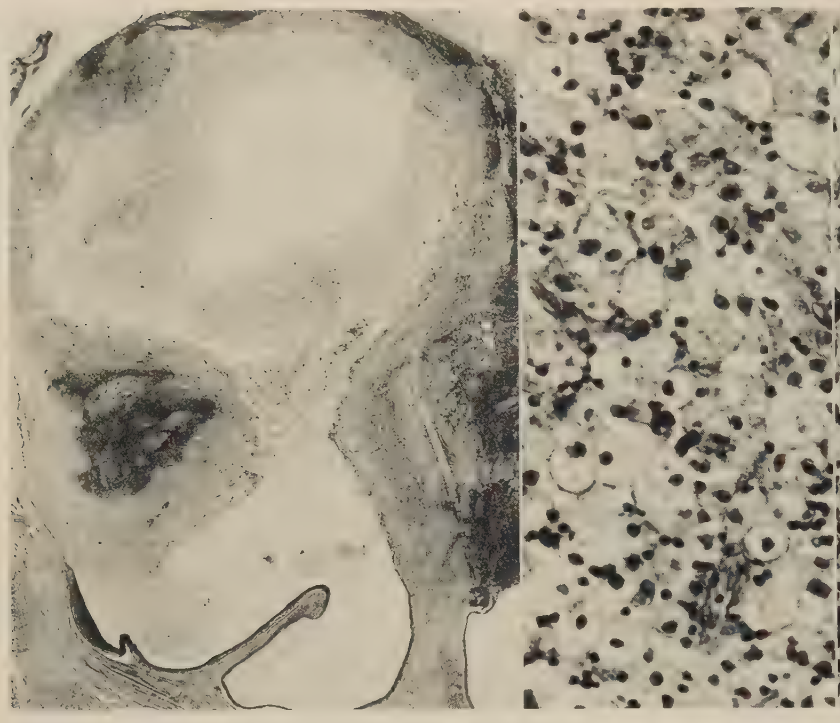
Fibrolipomatous polyp. Lobules of fatty tissue as well as fibrous tissue and thick-walled vessels, in a polyp of long standing. x 20.



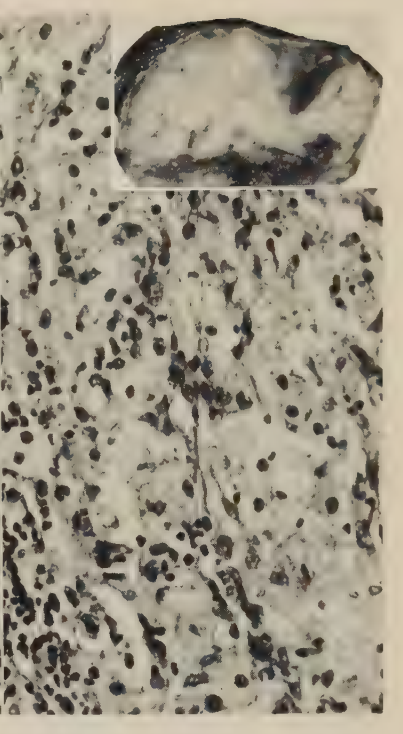
Cyst of probable branchiogenic origin. Tonsillar follicles and a crypt are recognizable. x 12. **Ciliated respiratory epithelium** lines the cyst, which contains mucinous material and cellular debris. Surface squamous epithelium of tonsil, at top. x 400. Such a cyst is considered attributable to a branchial or upper respiratory entodermal inclusion. (W. Dolan, Arlington, Va.)



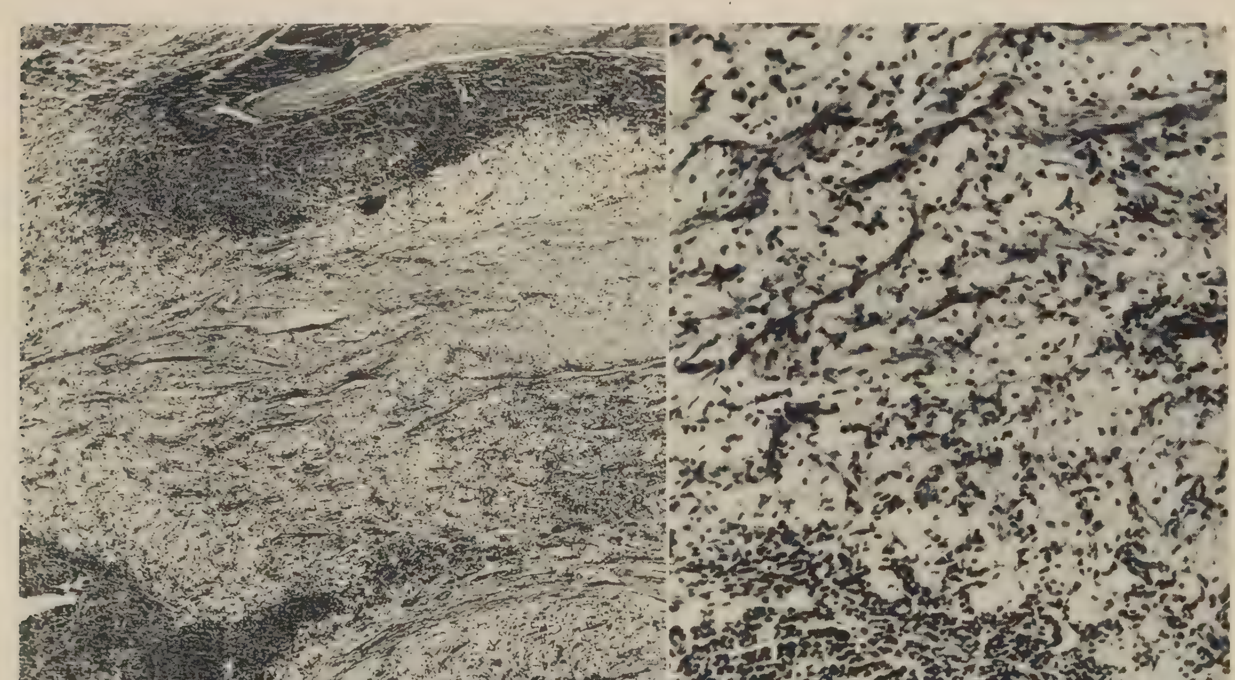
Epidermoid cyst. Cyst formed possibly by the isolation of an invagination of surface epithelium in crypt development; an epithelial inclusion, or inflammatory obliteration of crypt orifice. It is lined by **stratified squamous epithelium** and filled with debris and cholesterol. x 9, x 75.



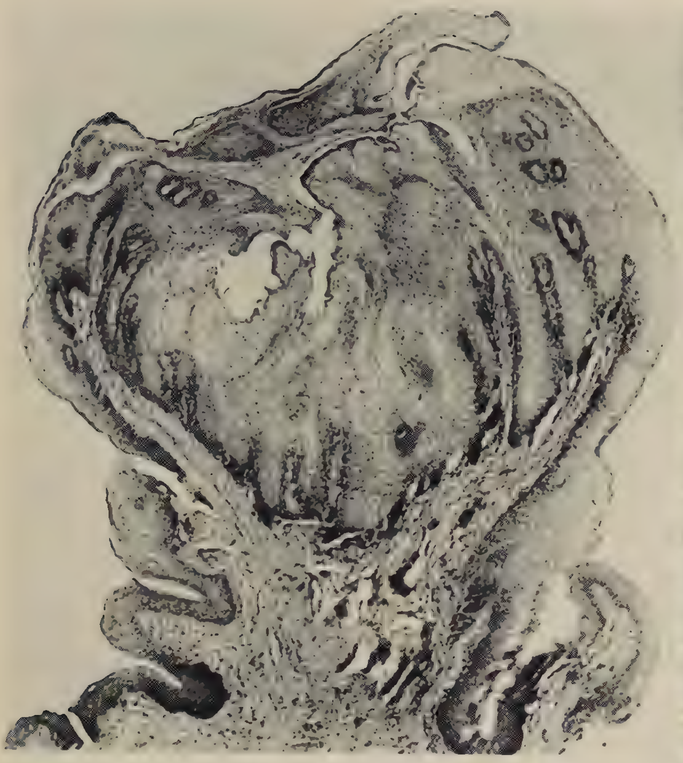
Biloculated epidermoid cyst of tonsil with intact squamous epithelial lining below. Accumulations of foamy macrophages, resembling xanthoma cells, form lining and contents of the upper part of the cyst and extend into the surrounding tonsillar tissue. x10, x310. (V.L. Cabaniss, Roanoke, Va.)



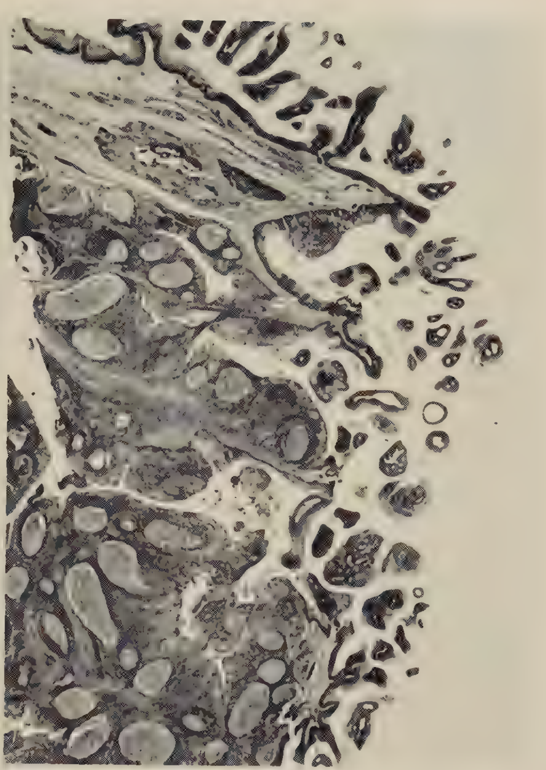
"Lipophagic granuloma" occupying a third of tonsillar mass *(inset)* and composed of xanthoma-like cells, may be end result of a cyst with no remaining evidence of an epithelial lining. x260.



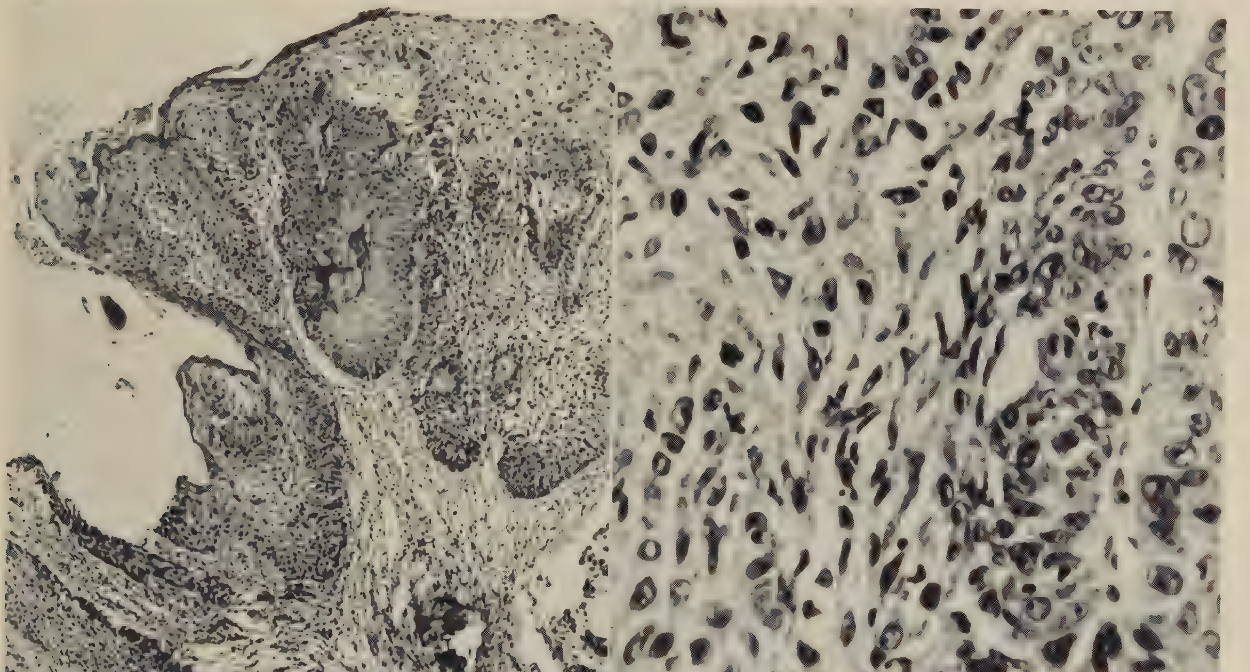
Xanthomatous reaction, etiology undetermined. Xanthoma cells diffusely infiltrating the tonsil of a 5 year old boy. Interpreted by competent pathologists as evidence of a systemic lipid histiocytosis, probably Hand-Schüller-Christian disease. x48, x210. No other lesions appeared, and the child is living and well eight years later.



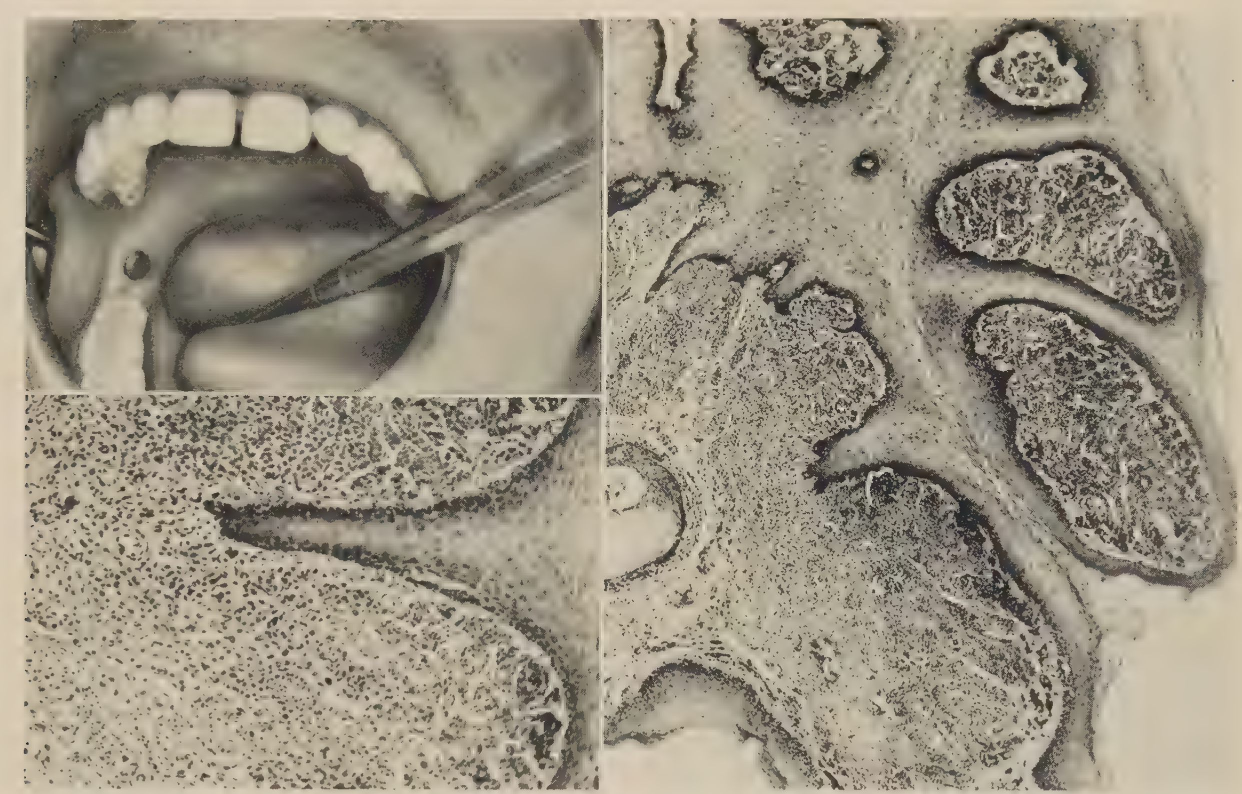
Inverted papilloma, clinically a firm verruca-like lesion, from the tonsillar pillar of a 28 year old woman. The "ingrowing papilloma" architecture of this lesion is more commonly seen in lesions of the nose. Benign. x40.



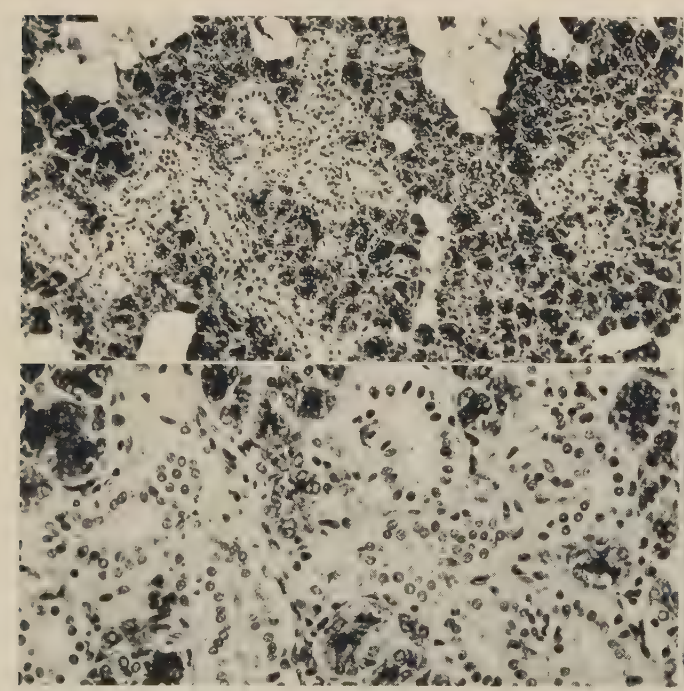
Multiple papillomas on surface of tonsil of a young boy, with involvement of adjacent oropharyngeal mucosa. Many delicate papillary stalks are seen in cross section. x10.



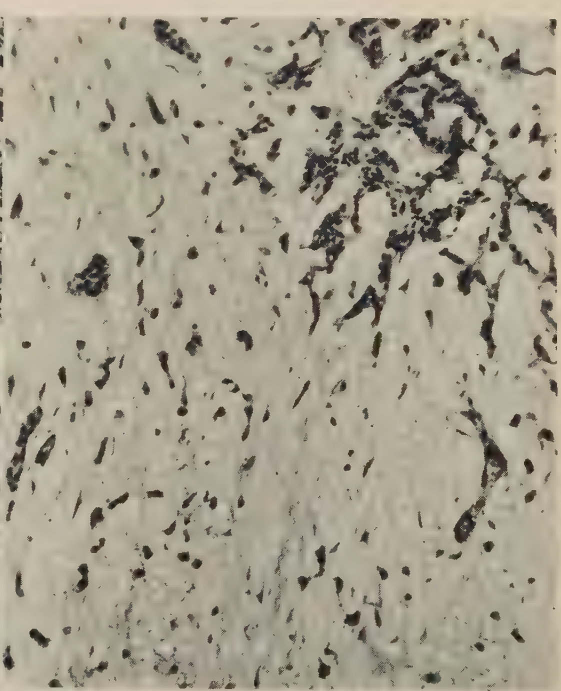
Acanthosis and dyskeratosis in a lesion, clinically "papillomatous," from the tonsil of a middle-aged man. Note cells with hyperchromatic nuclei, loss of polarity and numerous mitoses in *right* figure. x75, x355.



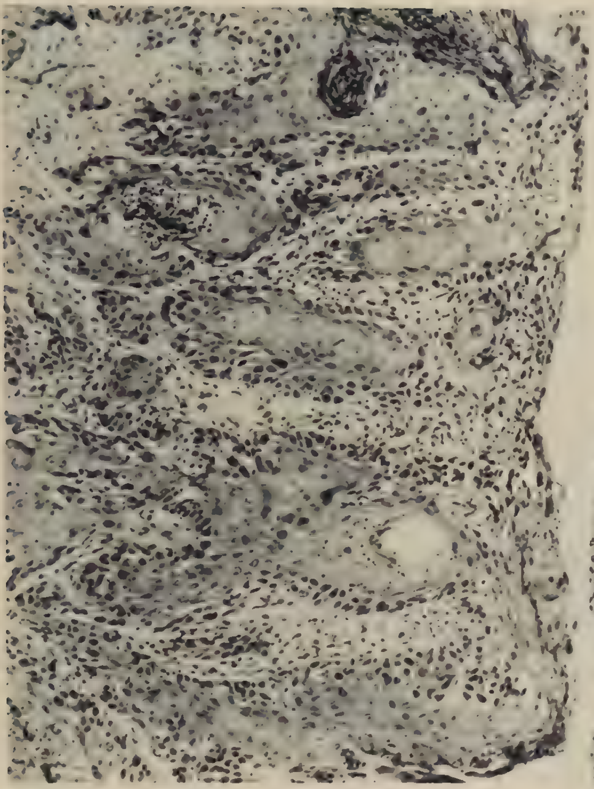
Intradermal nevus, anterior pillar, right tonsil of adult male. The surface of this very cellular pigmented lesion is papillary in contour. The nevus cells are in contact with the surface epithelium but are not within it. This is an "ectopic" benign intrademal nevus. x 80, x 48. (A. D. Alexander, Norfolk, Va.)



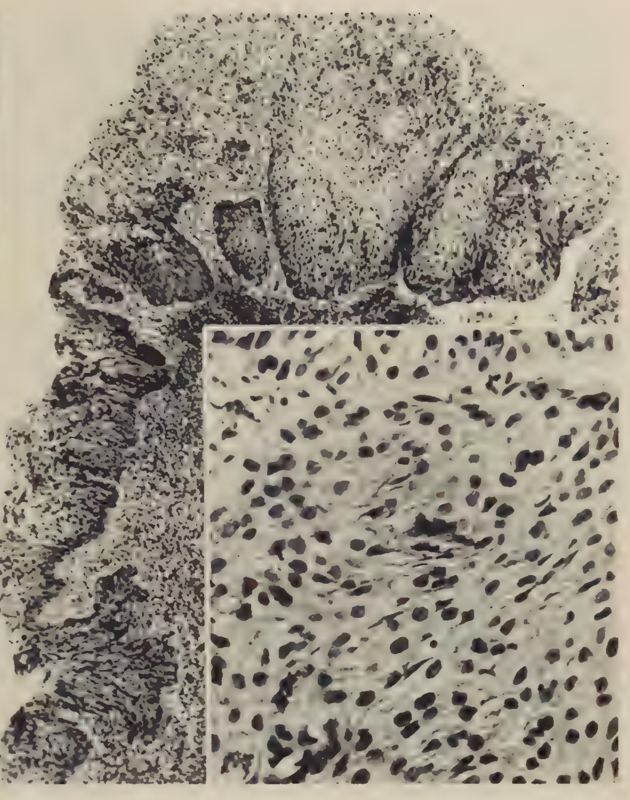
Ductal hyperplastic focus in an accessory salivary gland in the tonsillar bed resembles the epithelial portion of the Warthin tumor. There is no lymphatic tissue element, however, and while it may be a variant of that dysplastic tumor, it probably will not grow. x 75, x 185.



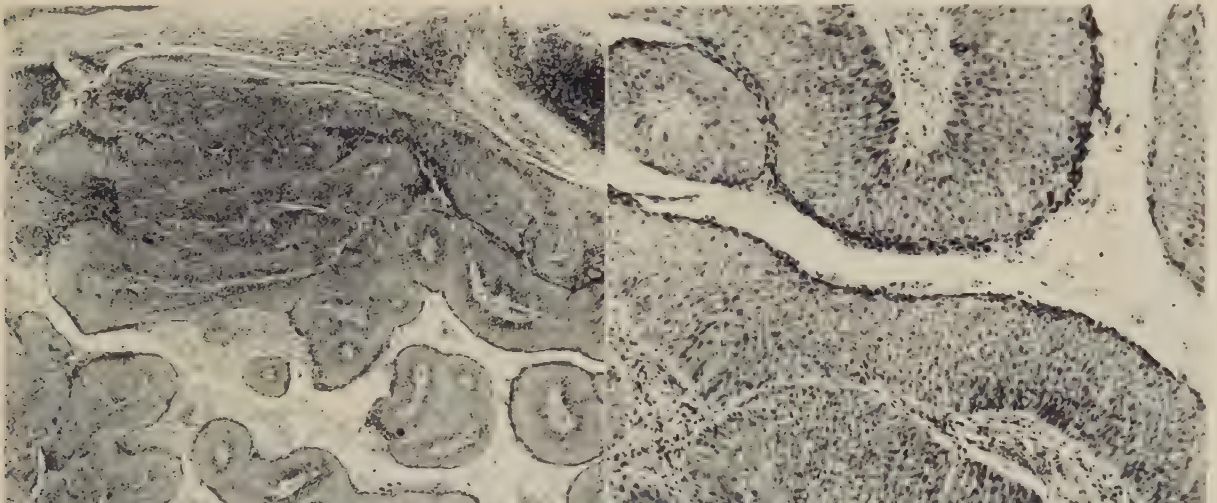
Mixed tumor of salivary gland type present for 6 months in the paratonsillar tissue of a 29 year old woman. The epithelial element shows a tendency to form acini; the mesenchymal portion appears more fibrous than usual. x 145. No subsequent record.



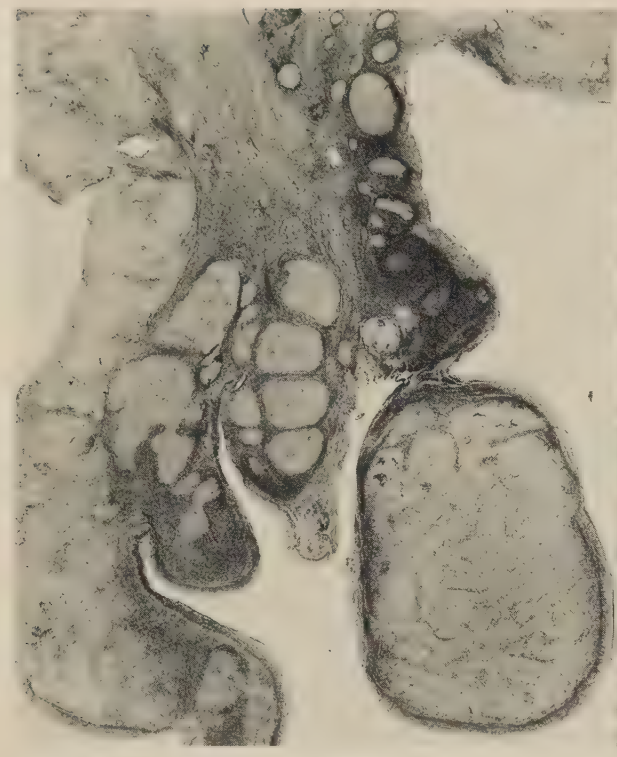
Epidermoid carcinoma, with keratinization, of tonsil and pillars, superficial but invasive, from a 52 year old man with sore throat for two weeks. He died of an unrelated bronchogenic carcinoma. x90.



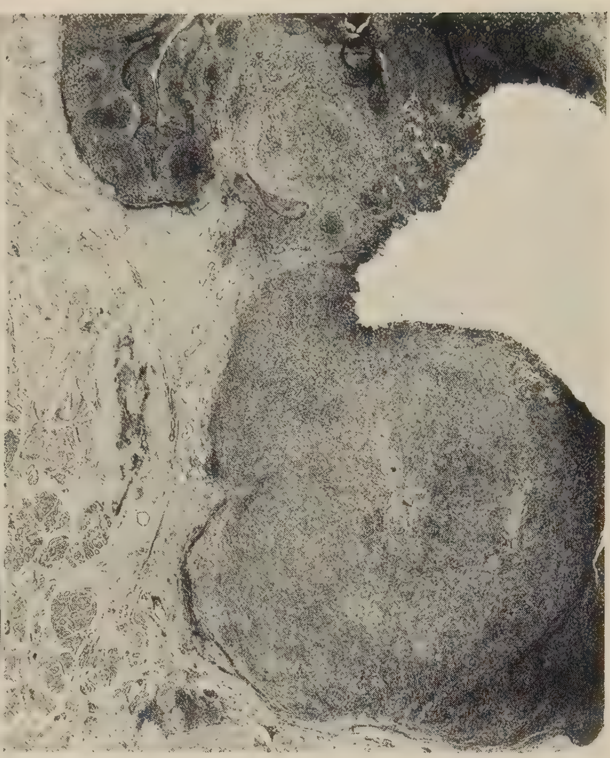
Extensive, superficial carcinoma of tonsil, pillar and oropharyngeal wall was diagnosed leukoplakia on several biopsies of a persistent ulceration. x55. Frank invasion of stroma in many areas *(inset)* by poorly differentiated carcinoma. x260.



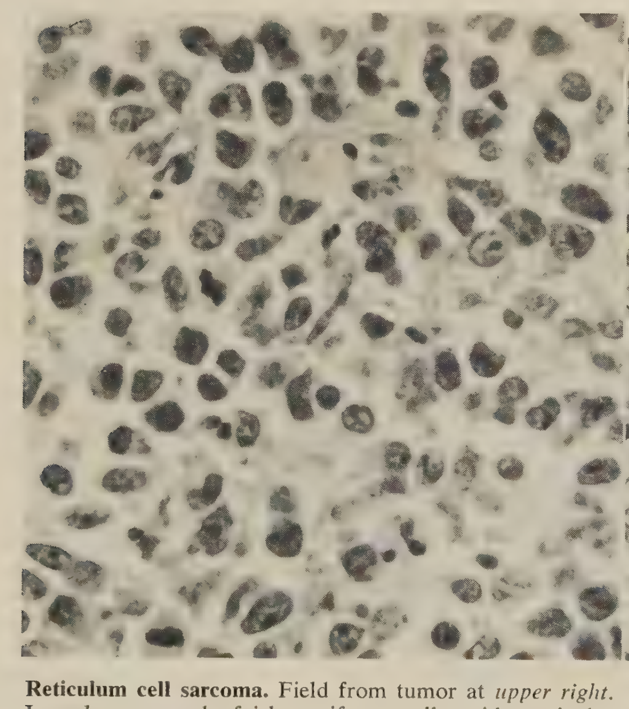
Papillary carcinoma. Biopsy from a 41 year old man, one month after painless swelling of cervical nodes and sore throat, diagnosed as peritonsillar abscess. Tonsillar and cervical tumors disappeared after irradiation therapy, but cranial involvement was the cause of death eighteen months after biopsy. *Left:* surface of tonsil at top. Diffusely infiltrating tumor was present in other areas. x28. *Right:* nonkeratinizing carcinoma of uniform cell type. x90.



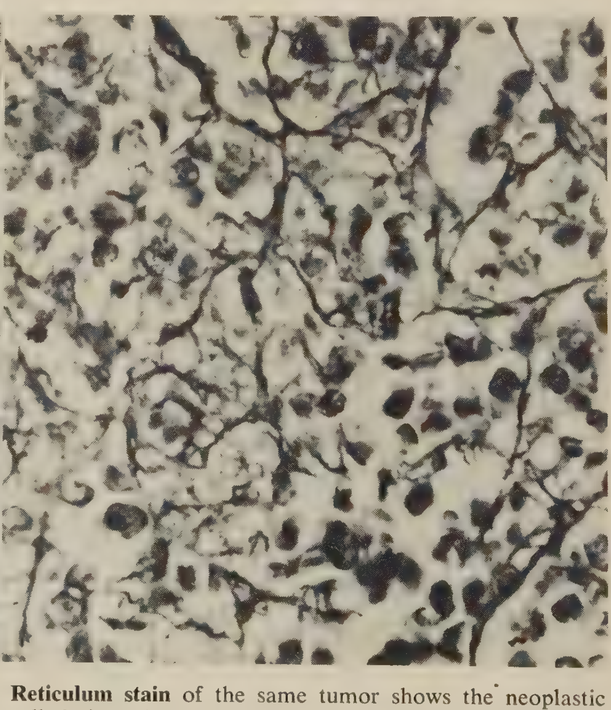
Origin in giant follicle lymphoblastoma is suggested by the exaggerated follicular pattern. Tonsil removed three weeks after cervical lymph node enlargement in a 57 year old man who died seven months later with generalized lymphoma, reticulum cell sarcoma type. x8.



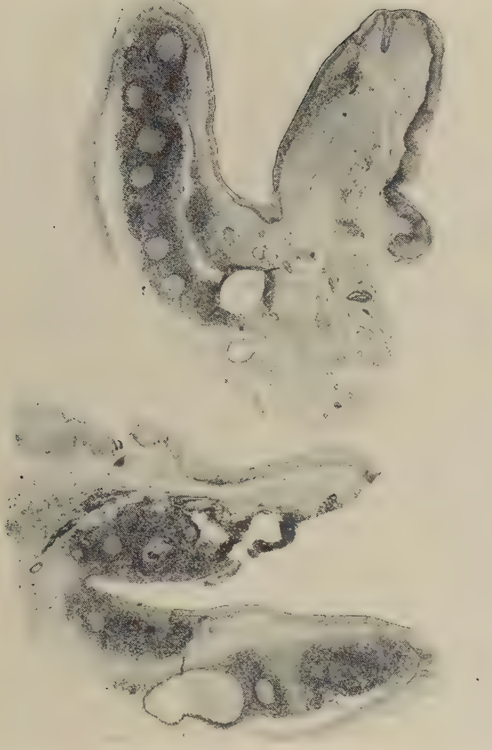
Follicular architecture erased by diffuse proliferation of neoplastic reticulum cells. Tonsil (3x3 cm.) in its fossa, the frequent site of quinsy, from a 55 year old woman. x7. No local recurrence a year later; died the following year of "renal cancer." (J. Budd, Los Angeles.)



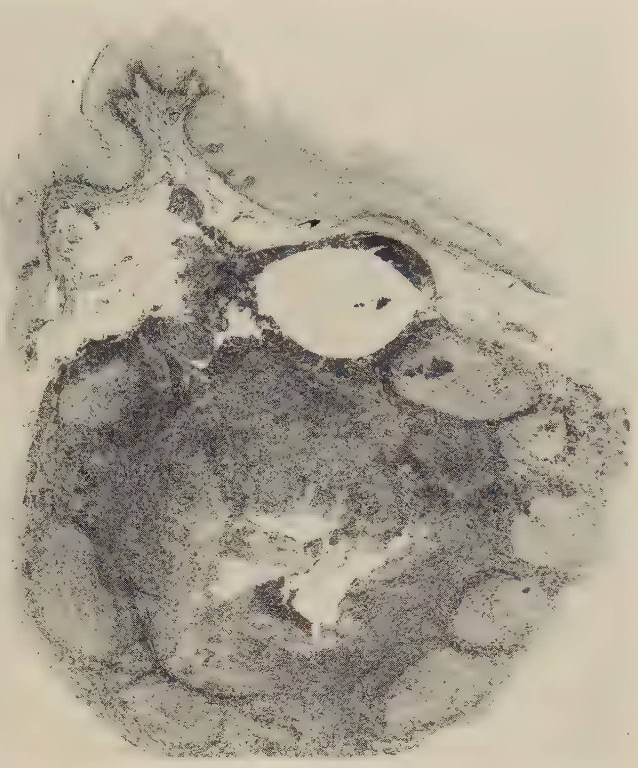
Reticulum cell sarcoma. Field from tumor at *upper right.* Loosely arranged, fairly uniform cells with vesicular round, oval, or indented nuclei with distinct nuclear membrane; moderately abundant cytoplasm; numerous mitoses. x700.



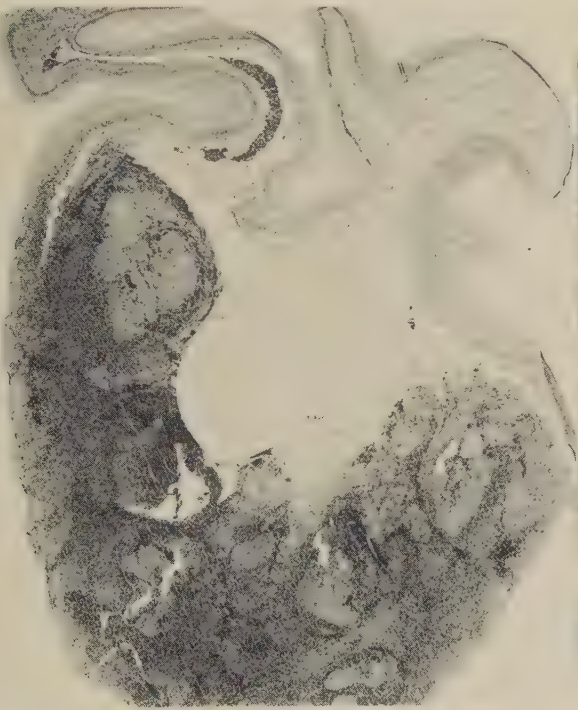
Reticulum stain of the same tumor shows the neoplastic cells intimately related to a network of branching reticulin fibers. x700. Though considered characteristic, this pattern is not always present.



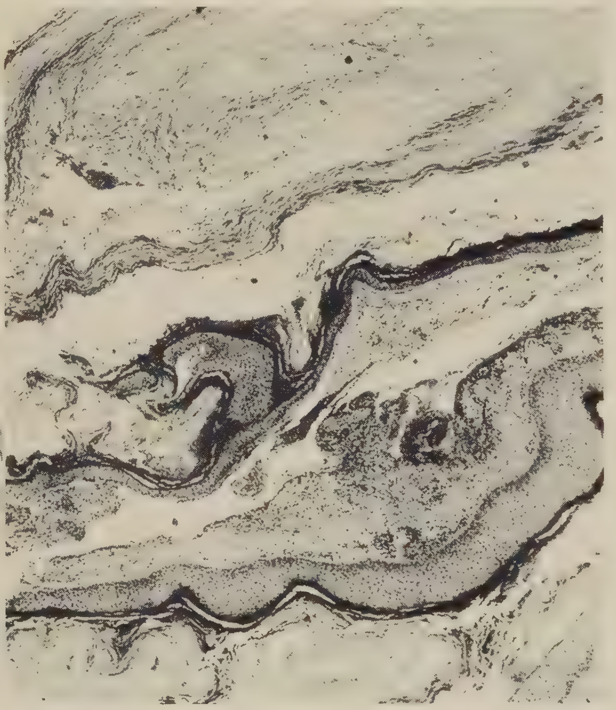
Papillary hyperplasia, with elevation well above surface at base of tongue, caused discomfort to 60 year old man. Cystic dilatation of crypt at bottom. x13. (H.F. Anderson, Wash., D.C.)



Chronic inflammation. Reactive hyperplasia of lymphatic tissue; purulent exudate and blood in ulcerated crypt. Section adjacent to the abscess shown in *lower left* from a 72 year old woman. x33. (L. Schwartz, New York, N.Y.)



Abscess produced a "lump" on left side of tongue in elderly female, fearful of cancer. Overlying lingual mucosa, forming part of abscess wall, collapsed into cavity after evacuation of 8 cc. of pus at operation. x31.



Epidermoid cyst lined by squamous epithelium and filled with keratin, removed from base of tongue of a 57 year old man. Dull pain in throat and face and hoarseness had been present for several months. x39.

CHAPTER 24

LARYNX

NORMAL HISTOLOGY

The gross anatomy of the larynx is adequately covered in the standard texts and will not be repeated here. It is necessary, however, to mention some of the normal histologic features because they have a bearing on the pathologic changes.

Mucosa.—Both surfaces of the epiglottis are covered by squamous epithelium, although patches of ciliated epithelium and taste buds are found at times on the laryngeal surface. That on the lingual, anterior surface shows abortive rete pegs, simulating those of skin, but that on the dorsal or tracheal surface has a smooth basilar layer. The cavity of the larynx is lined by ciliated respiratory epithelium, with the exception of the true vocal cords and the aryepiglottic folds which are covered by squamous epithelium. The respiratory type of epithelium continues on through the trachea into the bronchi. The motion of its cilia is such as to produce a current toward the mouth.

MUCOUS AND SEROUS GLANDS, predominently the former, are present in the mucosa of the entire respiratory tract except in that of the true cords. The glands are particularly numerous in the false cords and in the ventricles. All of the epithelial mucosa has a definite basement membrane, but there is some variation in the amount and character of the stroma in the different portions. It is relatively abundant and of looser texture on the anterior surface of the epiglottis, in the aryepiglottic folds and portions of the glottis, while in the deeper larynx there is relatively little. This is of practical significance, for angioneurotic and allergic reactions are more intense in the looser portions of the mucosa. There are elastic fibers in the subepithelial mucosa (tunica propria) and these are particularly prominent in the true cords, where by special stains they can be demonstrated in two separate layers, the delicate superficial layer close to the epithelium and a dense, deeper layer that is intimately associated with the striped muscle of the true cord, the thyro-arytenoid muscle.

The thyroid, cricoid, and the lower parts of the arytenoids are hyaline cartilage and as such tend to become more or less ossified with advancing age. The remaining cartilages are of the white fibroelastic type.

An important detail in the structure of the true cord is REINKE'S LAYER which lies between the two sheets of elastica, parallel to the long axes of the cords, limited above and below by the linea arcuata superior and inferior. These are linear depressions on the upper and lower margins of the cord, about 2 mm. from its free edge, and they appear to be a factor in limiting pathologic processes to the free edges of the cords. Reinke's space is scarcely identifiable in the normal cord, but in inflammatory states it becomes greatly thickened from edema. This facilitates biopsy without damage to the cord.

The laryngeal ventricle is the ovoid depression between the true and false cords. It is lined by a thin layer of respiratory epithelium that is loosely applied to the perichondrium of the thyroid cartilage. The protruding fold of the mucosa contains more or less lymphatic tissue and is called the laryngeal tonsil.

A congenital malformation that should be mentioned is the LARYNGOCELE. It is a diverticulum of the mucosa of the laryngeal ventricle which may remain entirely within the larynx—internal laryngocele—or may protrude through a defect in or dissect above the thyroid cartilage. It may extend into the neck and produce swelling on one side of the midline. It becomes filled with air or mucus which sometimes can be expressed into the larynx by external pressure. Such formations are normal in some of the lower species, especially certain monkeys. The laryngocele is lined by respiratory epithelium. The lesion is represented in the Registry by several cases. One of these is an external laryngocele from a 38-year-old man who, for many years, had been aware of a soft swelling below the angle of the jaw on the left side. It filled with air when he coughed and could be emptied by external pressure, producing a whistling sound within the mouth. It had never been inflamed.

Ventricular hernia (prolapse) is a bulging of the mucosa of the ventricle as a rounded, soft mass between the cords. It is due to infiltration of the mucosa by exudate. Syphilis was formerly considered to be the commonest cause, but that is not the present experience. Tuberculosis is a possible factor.

LARYNGITIS

Laryngitis is usually an extension of an acute inflammatory reaction from the upper respiratory tract; it may be on a traumatic basis and localized, following excessive and improper use of the voice, or it may result from inhalation of irritating fumes. The larynx, of course, suffers intensively with the bronchi from the inhalation of flames and hot gases, and burns of varying degree occur, including superficial destruction and charring.

The pathology of the acute inflammatory processes is the same as that in other upper respiratory mucosae, namely, congestion, a certain amount of edema, a limited amount of cellular exudate of the small mononuclear type, and more or less increased activity of the mucous glands. If the inflammation has been caused by irritating fumes or actual flames, ulceration of the surface epithelium and petechiae or frank hemorrhages are the usual consequences.

When the reaction is the result of infection by streptococci, like tonsillitis, a pseudomembrane may develop on the mucosal surface. This pseudomembrane differs from that of diphtheria in that it is yellowish rather than grayish in color, more friable because of the scarcity of fibrin content, and not so intimately attached to the surface. There may or may not be a loss of surface epithelium.

The larynx, particularly the glottis and epiglottis, may be the seat of localization of an allergic urticarial reaction. This is a vasomotor phenomenon that results in intense edema with very little exudate. The edema may be of sufficient severity to cause grave dyspnea, even suffocation. The reaction at times occurs in the early stages of influenza and may complicate peritonsillar abscess, Ludwig's angina, and deep neck infections. The localization of the edema is influenced by the histologic architecture. Portions of the larynx have a looser and more vascular submucosa than others, and edema is naturally more intense in these areas, specifically the aryepiglottic folds and the false cords.

Acute laryngitis in children may be manifested clinically by stridor. The pathologic picture is the same, but because of the smaller space in the glottis and the looser and more actively vascular mucosa, free breathing is readily interfered with. This false croup must be differentiated clinically from the membranous croup of diphtheria.

Laryngeal diphtheria is covered in the general discussion of that disease in the section on the pharynx, and is illustrated by figures in the plates on the larynx.

ACUTE LARYNGOTRACHEOBRONCHITIS is a clinical entity seen in very young children, occasionally occurring in epidemic form in institutions. It is frequently a streptococcal infection. *Hemophilus influenzae* has been isolated in thorax and blood cultures in the most severe cases. The prognosis is serious because of the toxemia and the possibility of suffocation from the acute and intense swelling of the laryngeal mucosa. LeJeune and Bayon have called attention to the membrane, like that of diphtheria but reddish brown in color, which is an added factor in suffocation. The mortality rate has been favorably influenced by early tracheotomy, a warm humid environment, chemotherapy and the antibiotics.

The pathologic picture is that of an acute inflammation with a predominance of subglottic edema. The reaction extends well down into the bronchial tree. Respiratory embarrassment results not only from the edema of the glottis, but also from the inspissated material in the larynx, trachea and bronchi.

Inflammations of the Epiglottis.—Recently Miller has again called attention to inflammation limited to the epiglottis. In very young children he finds it the result of infection by *Hemophilus influenzae* and in adults, usually by *Streptococcus*. In children it must be differentiated from tracheobronchitis. The condition is more fulminant in children and requires prompt measures, frequently including tracheotomy. In adults the condition is more sustained and may result in extensive ulceration or abscess formation. Pathologically, in both infants and adults there is a fulminant vascular reaction with intense congestion and edema. Cellular exudate is not conspicuous in the uncomplicated *H. influenzae* infections, but in the streptococcal infections a purulent exudate and hemorrhages are introduced. Exclusive of ulceration and abscesses, the reaction may extend to contiguous structures.

Chronic laryngitis may be part of a chronic upper respiratory infection, a result of trauma, such as prolonged over-use of the voice and long-standing exposure to irritating fumes and dust, including tobacco smoke. On microscopic examination the mucosa of the larynx generally is thickened by chronic exudate consisting of lymphocytes and polymorphonuclear cells. There may be hypertrophy of the gland elements of the mucosa and general hyperemia. The reaction is usually more prominent in the active portions of the larynx—the true cords, the laryngeal surface of the epiglottis, and the arytenoid eminences. In the first situation it results in focal polypoid or fibrotic thickenings.

Atrophic laryngitis (laryngitis sicca) is somewhat analagous to the ozena of the upper respiratory mucosa and is characterized histologically by reduction in vascularity and in glands. The respiratory epithelium shows a tendency toward metaplasia to the squamous type.

Contact ulcer (kissing ulcer) is nothing more than areas of ulceration on portions of the true cords that meet during phonation. Apparently on a traumatic basis, it is a condition of adults. Unlike the laryngeal nodule, it occurs most commonly on the posterior portions of the cord with ulceration of the thin mucosa over the vocal processes of the arytenoid eminences. It is necessary to differentiate these ulcers from such specific granulomatous lesions as tuberculosis and syphilis.

GRANULOMATOUS INFLAMMATIONS

Tuberculosis, which is practically always a complication of active pulmonary disease, is the commonest cause of granulomatous inflammation of the larynx and is seen most frequently in middle adult life, rarely in children. The reported incidence varies greatly, depending on the type of pulmonary disease on which the reports are based. For example, it averages 3 per cent in incipient and early cases, and close to 100 per cent in a hospital for advanced and terminal cases. This would imply that direct implantation of bacteria is the common mode of infection. There is the possibility, of course, that an occasional case is the result of a blood-borne infection. Meyerson, in fact, considers this a frequent occurrence.

The posterior structures of the larynx are most commonly affected—the arytenoids, the interarytenoid space and, in addition, the vocal cords and the posterior surface of the epiglottis, all sites of impact of the sputum during coughing.

The lesions almost always become ulcerative in time, but there may be an early acute diffuse phase of congestion and subepithelial, nonspecific, cellular exudate before frank tubercles develop. This has been interpreted as an allergic episode. When conglomerate tubercles form, the infection usually extends deeply to involve the perichondrium and large, localized tuberculomas most commonly may be clinically evident in the interarytenoid space. The perichondrium of the epiglottis and arytenoids are usually affected and this not infrequently results in involvement and deformities of the cartilages. Meyerson noticed premature ossification of the affected cartilages, especially of the thyroid cartilage. There are usually recurrent episodes of edema that can be of sufficient severity to compromise breathing. The microscopic appearance of the tuberculous lesions does not differ from that of tuberculosis elsewhere.

Syphilis involves the larynx in congenital infections, when it produces uniform and symmetrical hyperplasia, particularly of the epiglottic and arytenoid mucosa. In acquired syphilis the mucous patch is the commonest manifestation and it does not differ from similar patches in other parts of the respiratory mucosa. In the absence of lesions in the oral and upper respiratory tracts the identity of the laryngeal patch might be missed without the dark field examination of smears. Condylomas occasionally develop, particularly on the epiglottis, more rarely on the cords. Gummatous lesions are very rare, but when they do occur they can be very destructive because the cartilage as well as the mucosa will be involved. Healing of such lesions leads to marked deformity of the larynx.

Leprosy commonly involves the larynx and can cause death through suffocation. It is one of the few circumstances in which death is directly due to this disease. The lesions are usually of the nodular type, although neurogenous ulceration of the epiglottis is not uncommon. Tuberculosis is one of the most frequent complications when leprosy involves the larynx, and it confuses both the clinical and histologic pictures. Tuberculoid leprosy is uncommon in the larynx, so the appearance of tubercles showing caseation can generally be interpreted as evidence of a tuberculous complication.

Fungus infections of the larynx are rare in this country, but are more prevalent in the South American and Central European countries. Occasionally blastomycosis of the larynx is observed, and in the absence of lesions elsewhere the diagnosis can readily be missed. A case in point is one in the Registry. A farmer in his fifties had had laryngeal difficulties for several years. A lesion was excised without significant improvement in the patient's condition. He was treated for tuberculosis for the succeeding two years, until biopsy revealed the true nature of the condition. He presented no evidence of lesions elsewhere.

Pathologically, blastomycosis is a granulomatous lesion with tubercle formation, causing widespread destruction of tissue and carrying the possibility of perforation of the laryngeal structures and fistula formation. The diagnosis depends on finding the budding spores, usually in the giant cells of the tubercles. As in the skin lesions, hyperplasia of the epithelium is a usual feature. Clinically and histologically this can simulate carcinoma. A case so diagnosed is included in the illustrations.

Pachydermia Laryngis.—One of the localized effects of chronic irritation is prominent hyperplasia of the squamous epithelium of the true cords and of the interarytenoid space. This is evidenced clinically by a diffuse thickening of the cords and the mucosa of the posterior commissure, with an accentuation of the pearly color of the cords and some roughness of the surface produced by the exfoliating keratin.

Histologically, there is a great increase in the thickness of the squamous epithelium with accentuation of the rete pegs, usually a prominent pigmented granular layer, and an overlying layer of varying thickness made up of keratin flakes or parakeratotic cells. It differs from the picture in leukoplakia in that the epithelium is more uniform in thickness, dyskeratosis is absent, and the underlying inflammatory reaction is comparatively sparse. In some instances the epithelium has a verrucous character, i.e., it is thrown up into papillary projections by elongation of the underlying connective tissue stroma. There is usually more keratinization in this form than in the flat, smooth type. The differentiation between pachydermia and leukoplakia is of more than academic interest, because the former is a benign process and the latter is a potentially malignant one capable of eventuating in frank squamous cell carcinoma. The important criteria are the orderly arrangement and maturation of the cells and the scarcity of inflammatory reaction in pachydermia, and the dyskeratosis, atypical cells, and number of mitotic figures in the epithelium and the invariable inflammatory reaction in the underlying stroma in leukoplakia.

LARYNGEAL NODULE (CHORDITIS NODOSA)

While the laryngeal nodule is clinically a tumor, it is in fact a specialized reaction to trauma. It has been known under a variety of terms: polyp, fibroma, singer's or preacher's nodes, varices, and amyloid tumors. Ash and Schwartz, after investigating a large number of cases in the Registry, however, found it possible to follow the development of these lesions from an origin of fibrous hyperplasia through a series of changes in which each of the various clinical terms is applicable at some stage.

In practically every instance there was a specific history of misuse or excessive use of the voice and only occasionally was there a history of noteworthy inflammation of the upper respiratory tract. The lesion is characterized clinically by an absence of evidence of inflammation. In our experience it occurs predominantly in the male, in the proportion of five to one, and it is comparatively rare in Negroes. Holinger, however, notes that the singer's node *per se,* is twice as frequent in women as in men. He ascribes this difference in incidence to the fact that the singer's nodes are very small when removed and do not reach the pathologist.

In every instance the initiating symptom was hoarseness which persisted from months to several years. Many of the lesions studied by Ash and Schwartz were located on or about the anterior ends of the cords.

The lesion begins as a nodular thickening of the mucosa that histologically is seen to be caused by proliferation of fibroblasts in the stroma and thickening of the epithelium. This is the FIBROUS STAGE. The POLYPOID STAGE is most obvious in lesions on the edges of the true cords through involvement of Reinke's layer. The thin-walled vessels rapidly dilate and the edema increases until there is a well circumscribed tumor made up of exceedingly edematous, loosely fibrillar and poorly cellular stroma and enormously dilated, very thin-walled vessels. This is the VARIX STAGE. The final stage is the development of large masses of fibrinoid hyalin in the stroma, in the vessel walls, and even in the lumens of the vessels. It is this stage that has been called the AMYLOID TUMOR. The hyalin, however, is not true amyloid, but is produced by the fusion of fibrin and reticulin fibrils and probably also by the precipitation of colloid elements of the interstitial fluid. In none of the nodules in our series was amyloid demonstrated. (See color plate B.)

There is rough correlation between the duration and the pathologic type of the lesion. The early fibrous stage is seldom seen because the patient usually does not seek medical advice until after several months of hoarseness, but in several of our cases the lesion was still in this stage after five years. We interpret this delay as due to favorable anatomic conditions of the larynx and to a slighter degree of trauma.

There is, of course, a gradual transition from one stage to the other. In the second, or polypoid stage there is already an increase in the number and in the diameter of the blood vessels, and the hyaline material begins to accumulate noticeably in the stage of varix. The blood vessels of the cord normally run parallel to the long axes of the cords, but in the nodule the newer vessels extend toward the surface at right angles.

Several secondary changes are encountered, among them, hemorrhage. The vessels have remarkably thin walls and, until they are protected by the accumulating hyaline material, they would seem to be very susceptible to rupture. It is remarkable that hemorrhage is not more common.

In most instances the covering epithelium is moderately atrophic. Occasionally it is hyperplastic with large rete pegs, and the pattern may approach that of pseudoepitheliomatous hyperplasia, when it can be confused with squamous cell carcinoma. In only one of the 138 cases analyzed several years ago, however, was there frank carcinoma. In several instances the epithelium was of the pachydermal type.

Amyloid.—As mentioned in the discussion of the laryngeal nodule, the majority of the supposed amyloid tumors of the larynx are really not amyloid. The larynx does, however, share in the deposition of true amyloid in the rare condition of primary or idiopathic amyloidosis. The distribution in this disease is quite different from that seen in the more common amyloidosis that is a complication of chronic suppurative inflammation and of tuberculosis. Primary amyloidosis of the tongue is illustrated in Chapter 3.

The true amyloid deposits are not limited to the cords, as the laryngeal nodules usually are, but are more diffusely scattered in the mucosa as firm masses. The nature of the masses can usually be identified because of the amyloid deposits in other parts, especially in the skin and mouth.

PERICHONDRITIS

Bacterial infections may be sufficiently aggressive to extend through the mucosa and involve the perichondrium, resulting in deep-lying abscesses. It most commonly occurs in the thyroid cartilage above or below the cords. In the former situation the abscess may form in the pyriform fossa. This means, of course, that the abscess has eroded through the thyroid cartilage.

Other abscesses occur as complications of specific diseases, such as scarlet fever, erysipelas, and especially typhoid fever. In chronic granulomatous infections—tuberculosis, syphilis, and certain of the fungus diseases—involvement of the cartilages is evidenced by the development of conglomerate tuberculoid abscesses.

Perichondritis can follow traumatic, irradiation, or inflammatory destruction of the mucosa. Foreign bodies, instrumentation, and specific ulcerations (syphilis and tuberculosis) would be included in this category. Clinically there is usually extensive laryngeal edema and induration, fixation of the vocal cords, and respiratory obstruction.

The perichondrium becomes infiltrated with exudate containing polymorphonuclear leukocytes, which separates the fibers from the underlying cartilage. With the increased accumulation of exudate, the perichondrium is raised, the underlying cartilage is invaded and becomes necrotic. In the later stages repair elements consisting of granulation tissue and newly formed cartilages are introduced. Repair is never complete and there are usually permanent deformities of the involved cartilages.

As a sequel of typhoid fever the organisms localize in the cartilages and produce typhoid chondritis, analagous pathologically to the typhoid spine resulting from localization of the infection in the vertebrae. The specific nature of the infection can be detected by the presence of the large mononuclear cell (typhoid cell) rather than the polymorphonuclear reaction that indicates infection by the pyogenic bacteria.

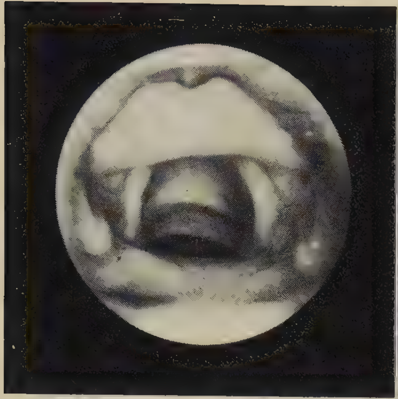
A rare dystrophy of the cartilages is represented by a case in the Registry in which not only the cartilages of the larynx, but also those of the nose and skeleton were involved. The case is cited in the section on the ear.

The muscles of the larynx are occasionally involved in trichinosis. The cysts may interfere with the normal function of the muscles. The larvae may be seen coiled within the muscle fibres and surrounded by a limited amount of chronic inflammatory reaction. If the larva dies it becomes calcified and there may be foreign body reaction with giant cells and epithelioid cells.

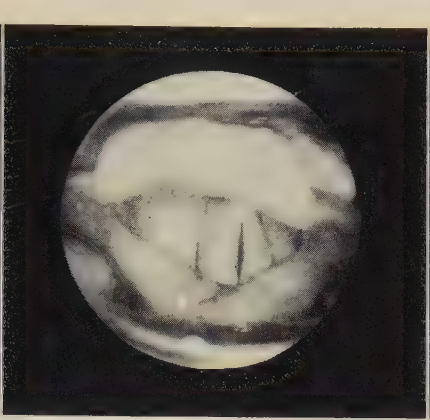
The cysts of echinococcus occasionally occur in the larynx on the arytenoepiglottic fold.

LARYNX

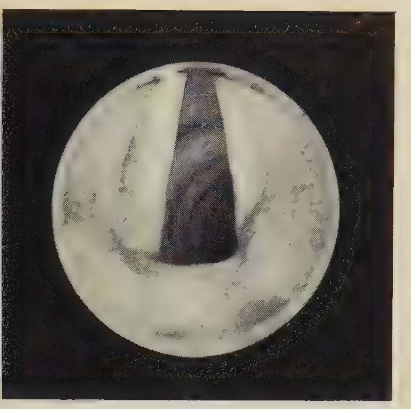
NORMAL IMAGE–HISTOLOGIC ANATOMY



Normal larynx during inspiration. Mirror view.

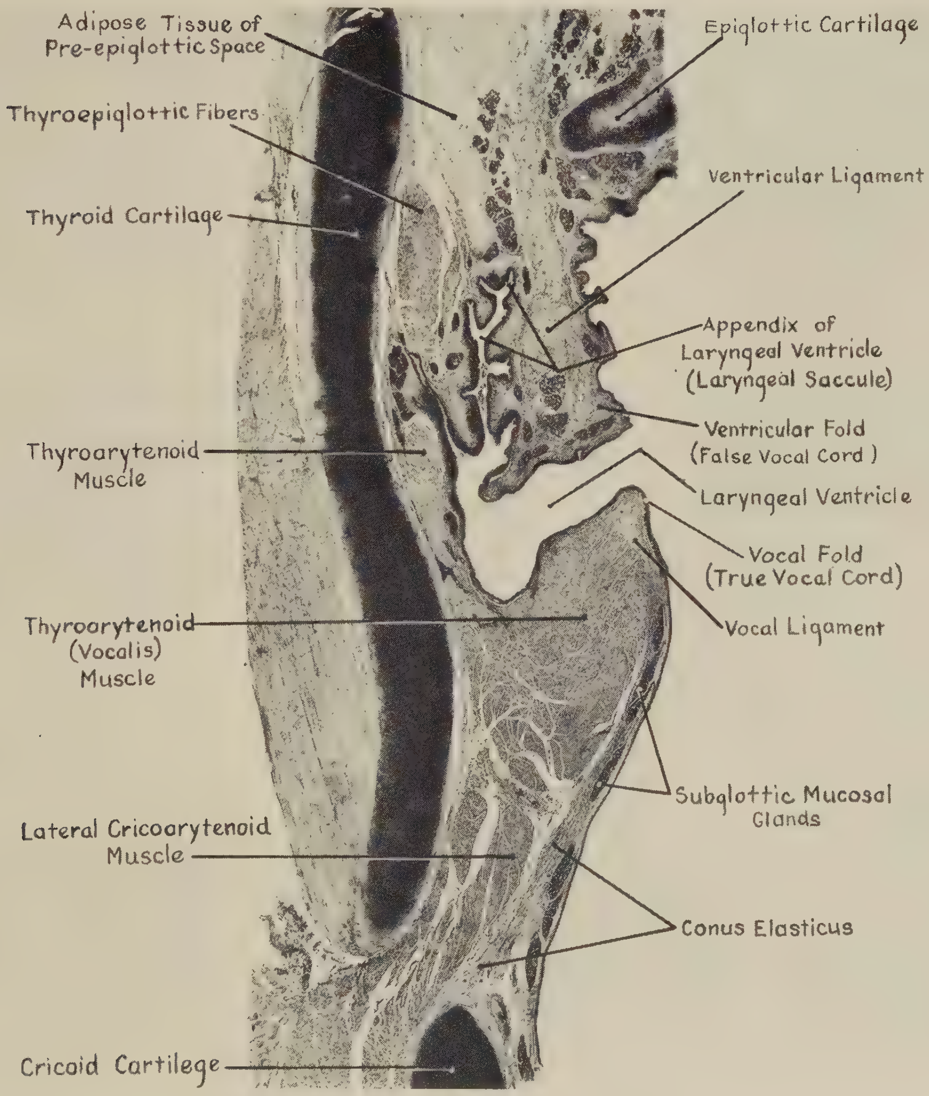


Normal larynx in phonation. Mirror view.

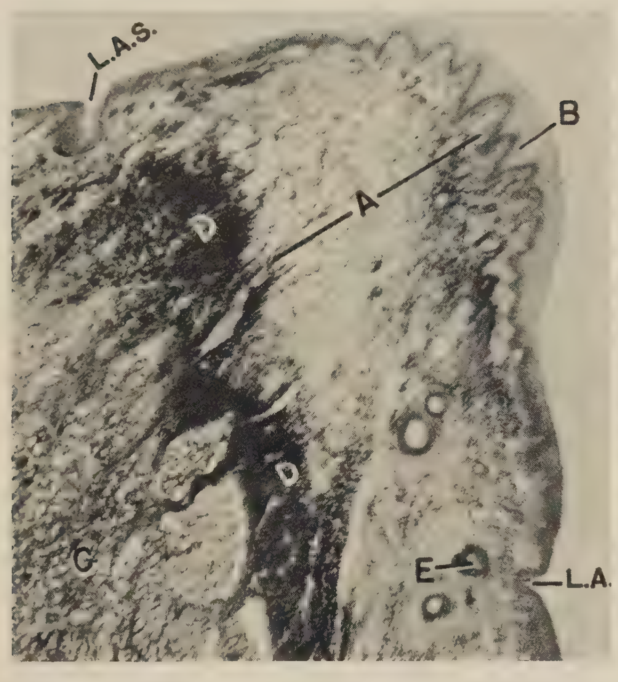


Direct laryngoscopic view of normal larynx.

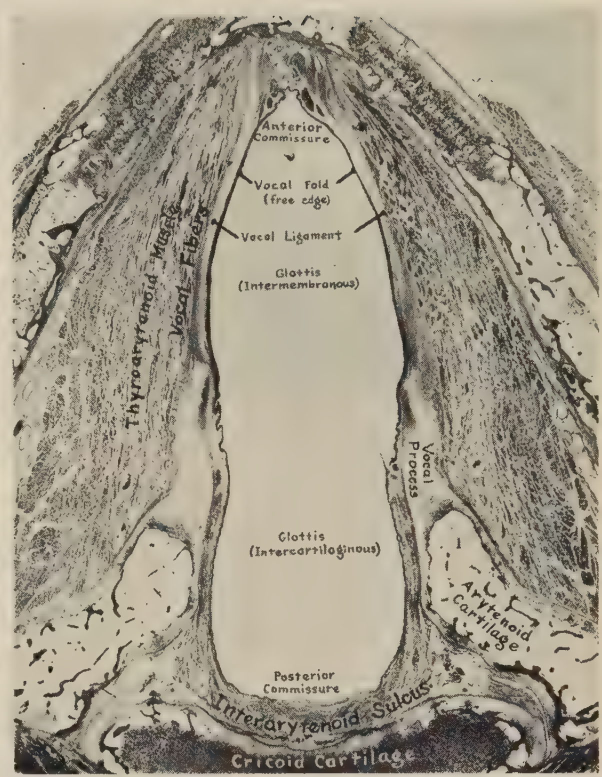
(All from P. Holinger, Chicago.)


Adipose Tissue of Pre-epiglottic Space
Epiglottic Cartilage
Thyroepiglottic Fibers
Ventricular Ligament
Thyroid Cartilage
Appendix of Laryngeal Ventricle (Laryngeal Saccule)
Ventricular Fold (False Vocal Cord)
Thyroarytenoid Muscle
Laryngeal Ventricle
Vocal Fold (True Vocal Cord)
Thyroarytenoid (Vocalis) Muscle
Vocal Ligament
Subglottic Mucosal Glands
Lateral Cricoarytenoid Muscle
Conus Elasticus
Cricoid Cartilege

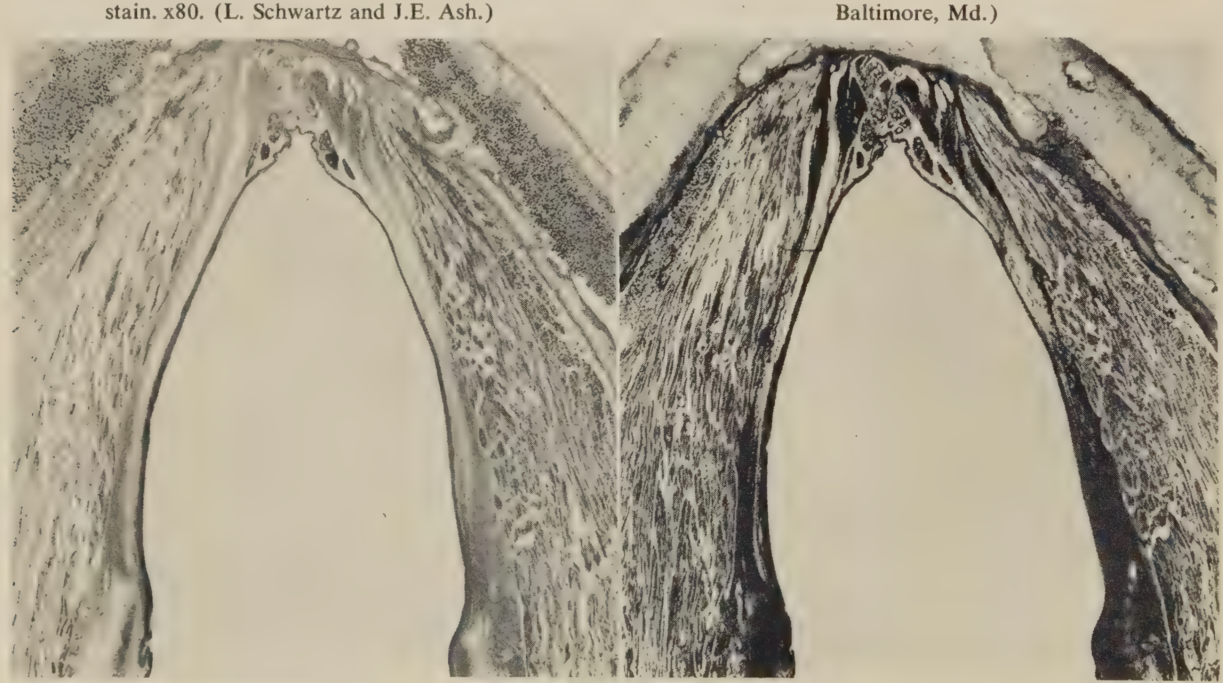
Longitudinal section of larynx through thyroid ala.
(F. Lederer, Chicago.)


L.A.S.
B
A
D
D
C
E
L.A.

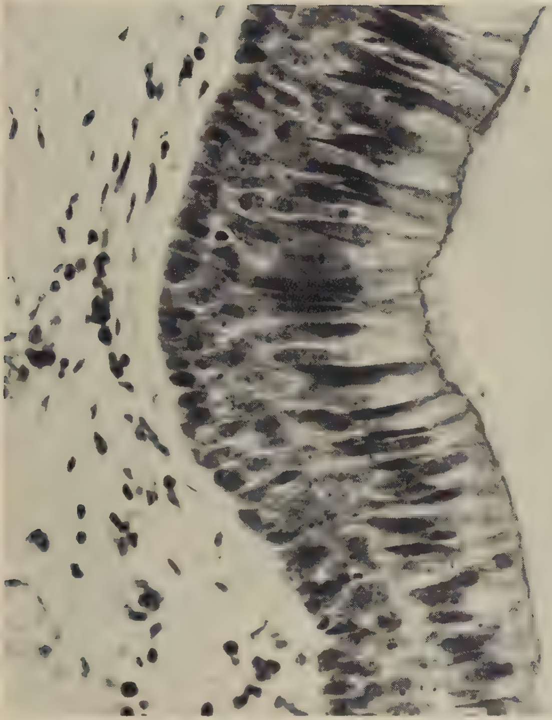
Vertical section through vocal fold (true cord). A, Reinke's space broadened by edema; **B,** normal squamous epithelium of cord is acanthotic; **C,** thyroarytenoid (vocalis) muscle; **D,** elastic fibers of the vocal ligament; **E,** duct of gland in subglottic mucosa (the true cord contains no glands; **L.A.S.** and **L.A.I.,** linea arcuata superior and inferior, boundaries of Reinke's space. Weigert's elastic tissue stain. x80. (L. Schwartz and J.E. Ash.)


Anterior Commissure
Vocal Fold (free edge)
Vocal Ligament
Glottis (Intermembranous)
Thyroarytenoid Muscle
Vocal Fibers
Vocal Process
Glottis (Intercartilaginous)
Arytenoid Cartilage
Posterior Commissure
Interarytenoid Sulcus
Cricoid Cartilage

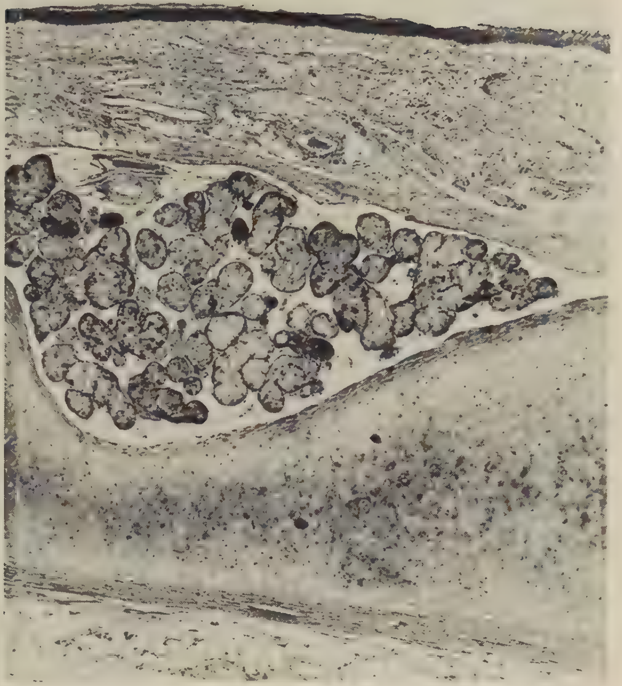
Horizontal section at level of vocal fold. Note ossification of the hyaline cartilages—thyroid, cricoid, and bases of arytenoids. x4. (Slide from S.R. Guild and S.J. Crowe, Baltimore, Md.)



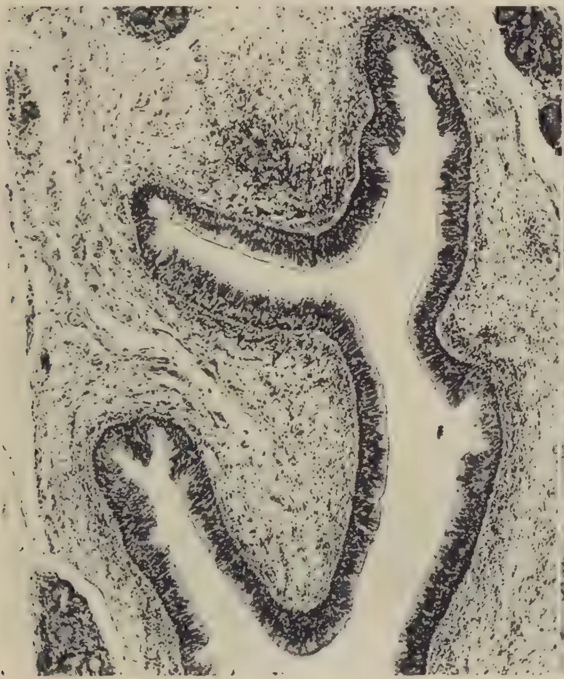
The vocal ligaments extend from the vocal processes of the arytenoid cartilages, with which their fibers fuse, to the midportion of the posterior surface of the thyroid cartilage. Horizontal sections through vocal folds (same case as *upper right*). *Left:* hematoxylin and eosin stain; *right:* elastic tissue stain. x7. The inferior margins of the vocal ligaments are continuous with the lateral portions of the conus elasticus, and they are thus considered the free borders of the latter. (S.R. Guild and S.J. Crowe, Baltimore, Md.)



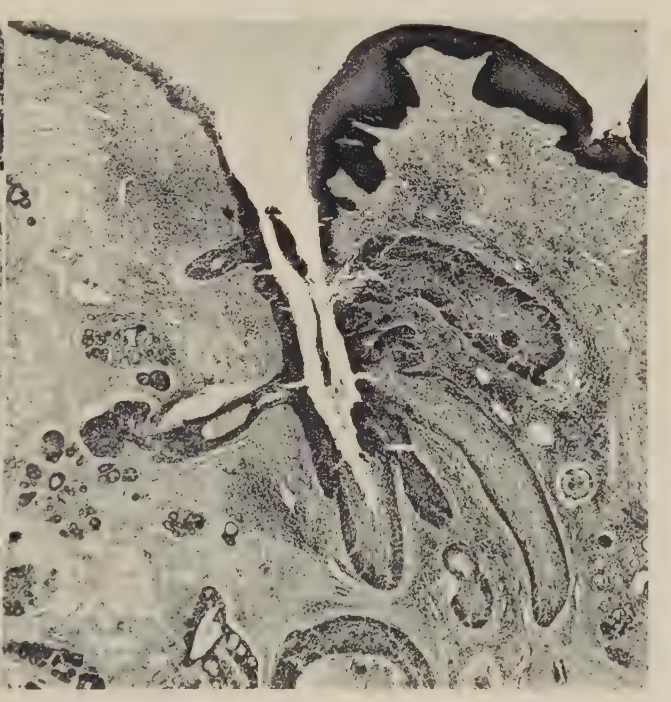
Ciliated pseudostratified columnar epithelium with distinct basement membrane lines most of larynx; squamous epithelium covers anterior and upper half of posterior surfaces of epiglottis, aryepiglottic folds and true vocal cords. x500.



Laryngeal surface of epiglottis. Firmly attached mucosa; squamous epithelium free of rete pegs. Mixed glands pit the elastic cartilage and its tightly adherent perichondrium. x35. Lingual surface has papillated epithelium; looser subepithelial tissue more subject to edema.

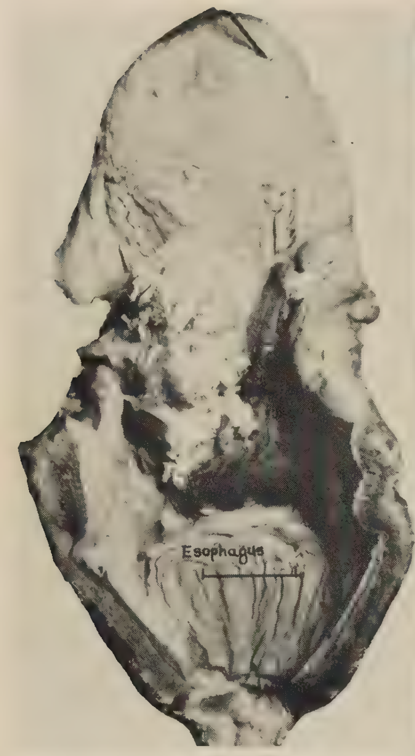


Appendix of laryngeal ventricle (laryngeal saccule). Like the mucosa of the ventricle—numerous glands and lined by ciliated respiratory epithelium. x100. (F. Lederer, Chicago, Ill.)

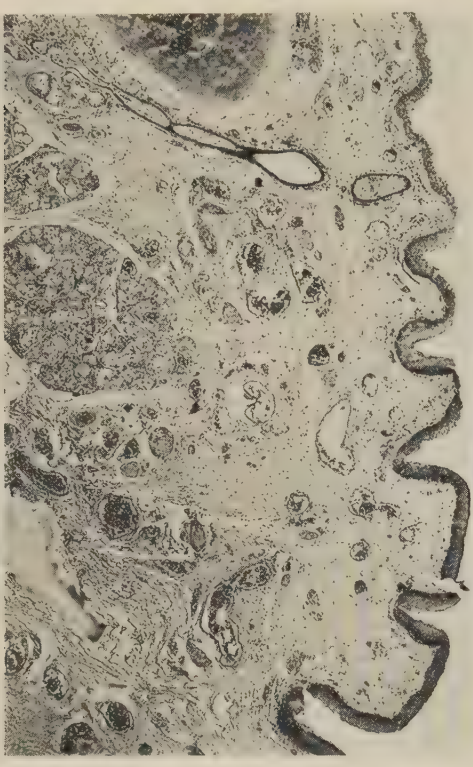


Epithelial hyperplasia and squamous metaplasia of laryngeal ventricle and its glandular ducts, due to chronic irritation. Hyperplastic true cord epithelium, upper right. False cord at left. x27. (W. Dolan, Arlington, Va.)

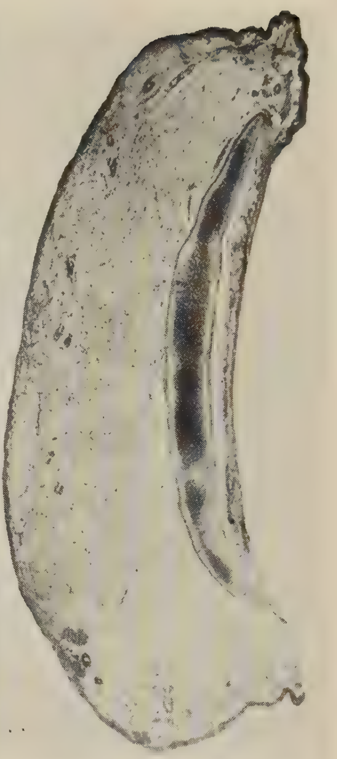
FOREIGN BODY—EDEMA—ACUTE LARYNGITIS



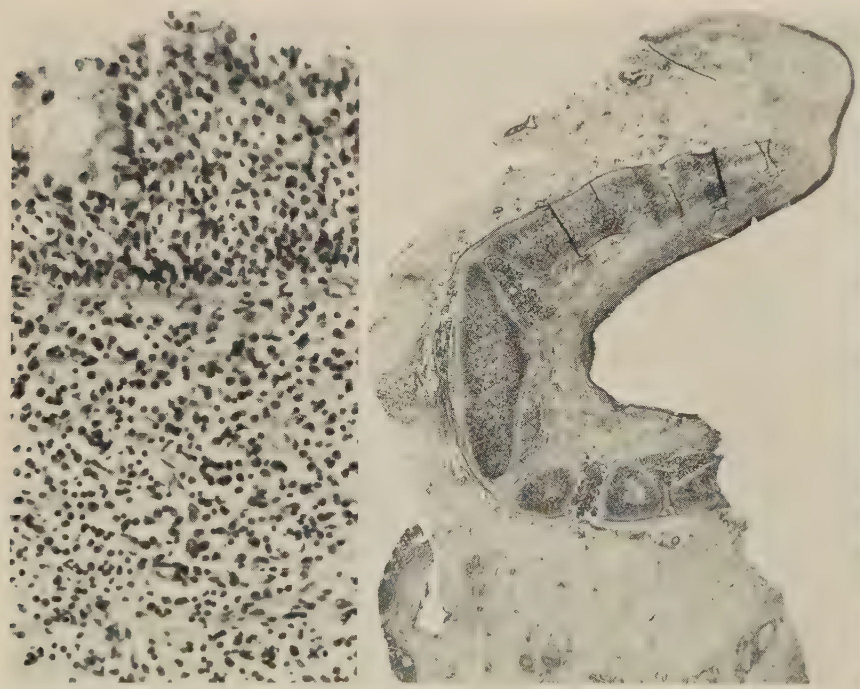
Foreign material (meat), impacted in larynx between pharyngeal wall and epiglottis, caused acute asphyxial death.



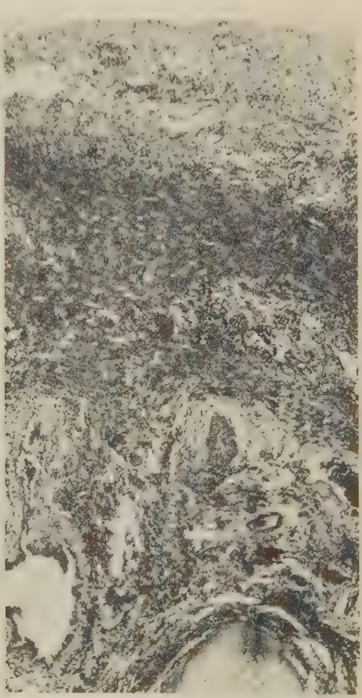
Edema and congestion of aryepiglottic fold in patient with peritonsillar abscess. Death during operation attributed to acute laryngeal edema. x27.



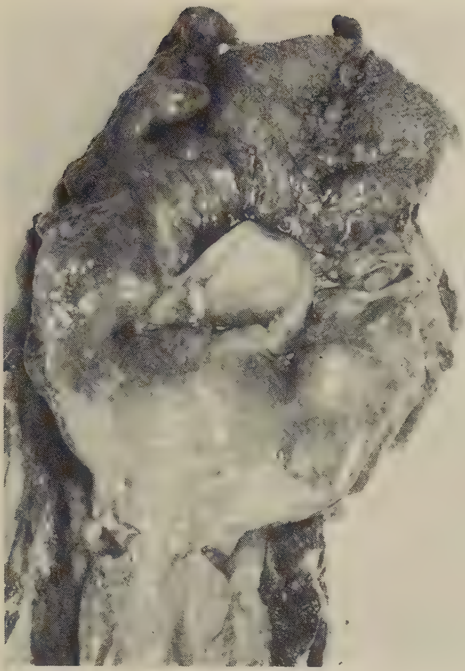
Edema of epiglottis, severe, typically limited to loose mucosa of lingual surface. Streptococcic cellulitis. x6.



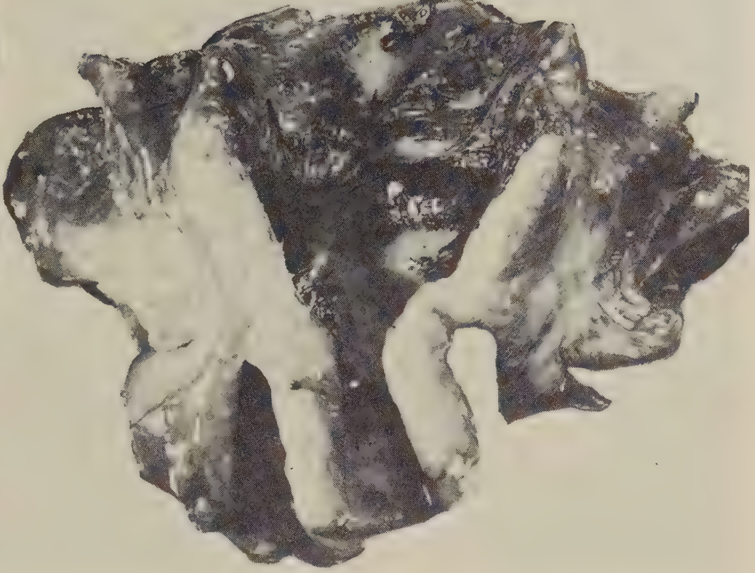
Acute laryngitis in fulminant streptococcic infection. Woman with sore throat and dyspnea died shortly after tracheotomy. *Left:* inflammatory cellular exudate, predominantly polymorphonuclear, in edematous mucosa. x150. *Right:* marked swelling, edema and congestion of lingual surface of epiglottis (partly torn). x6.



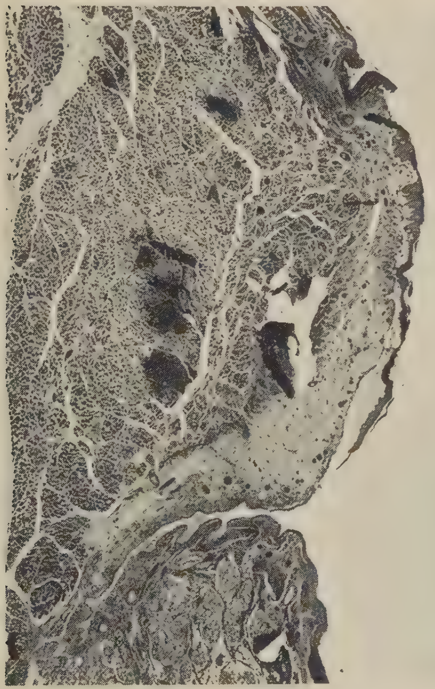
Diphtheria, epiglottis. Fibrin and hemorrhage in thickened, partly necrotic mucosa. x48.



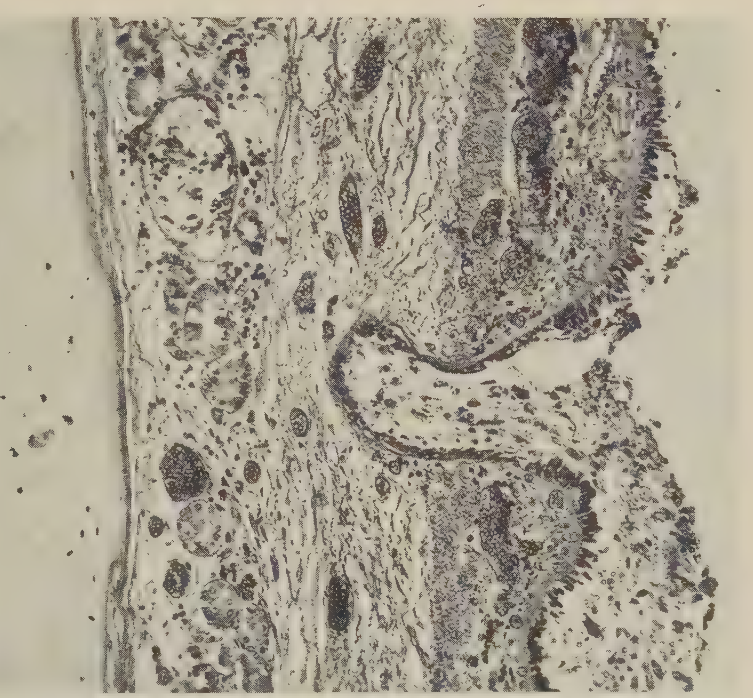
Flash burns of hypopharynx, as well as of face and body, as result of gasoline explosion in truck accident. Cyanosis relieved by tracheotomy; death on fifth day with "lower nephron syndrome." Note extensive edema and vesiculation.



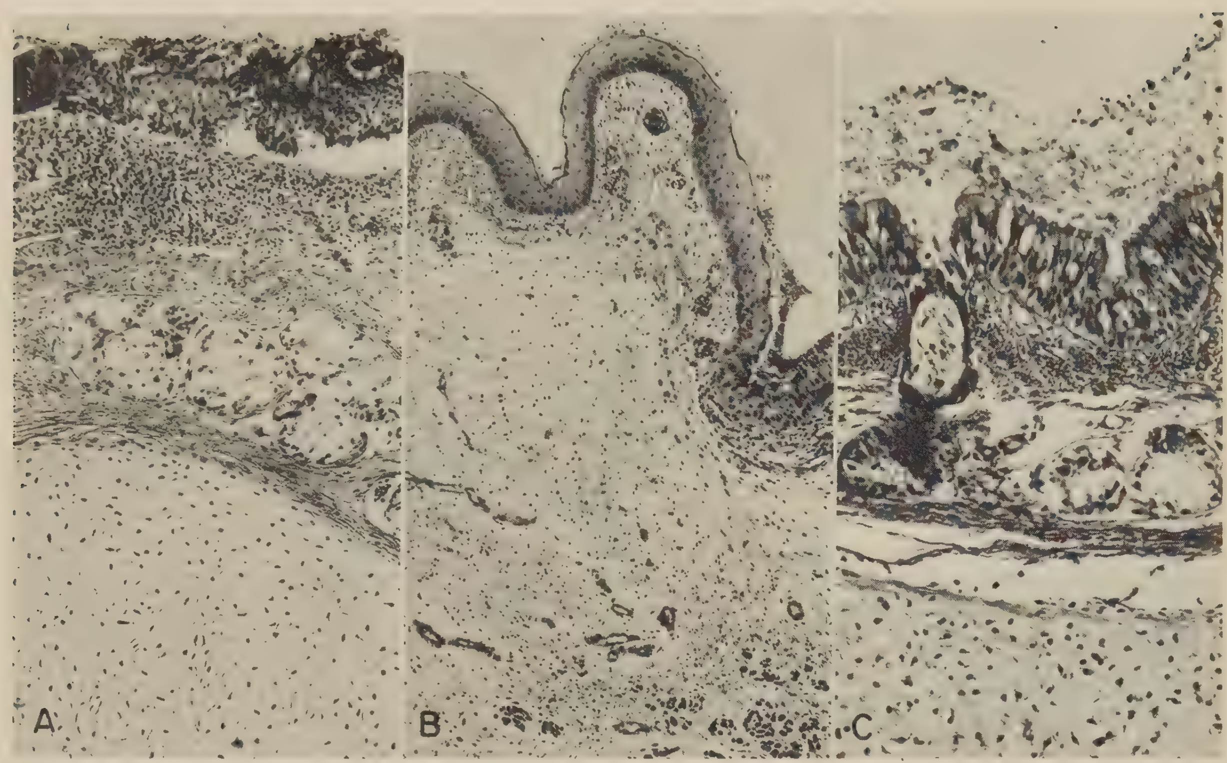
Severe burns of hypopharyngeal and surpraglottic tissues. Larynx of an inebriated 35 year old man, trapped and asphyxiated in a flaming building. Irregular erosions of mucosa, where castlike accumulations of charred brown-black exudate have been pulled away. Marked hyperemia and edema of subglottic mucosa.



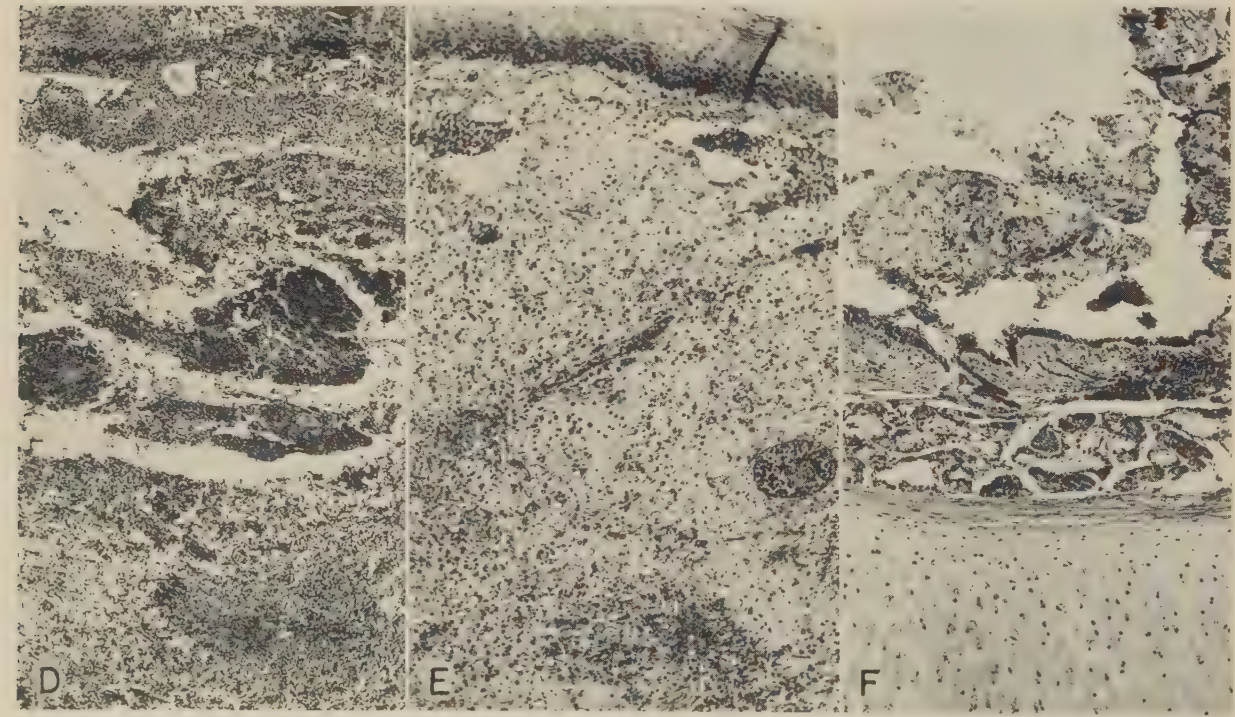
True and false cords in case at *upper right*. Vascular dilatation and congestion, focal hemorrhages, subepithelial vesiculation. x16.



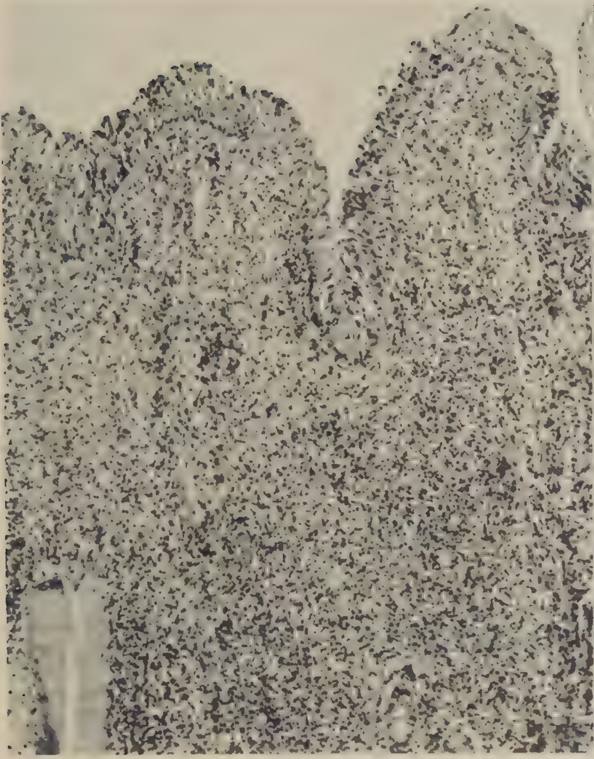
Subglottic and tracheal mucosa also appeared poorly stained, though less severely damaged. Edema; hyperemia; epithelial desquamation; granular cytoplasmic changes in degenerating cells. x114.



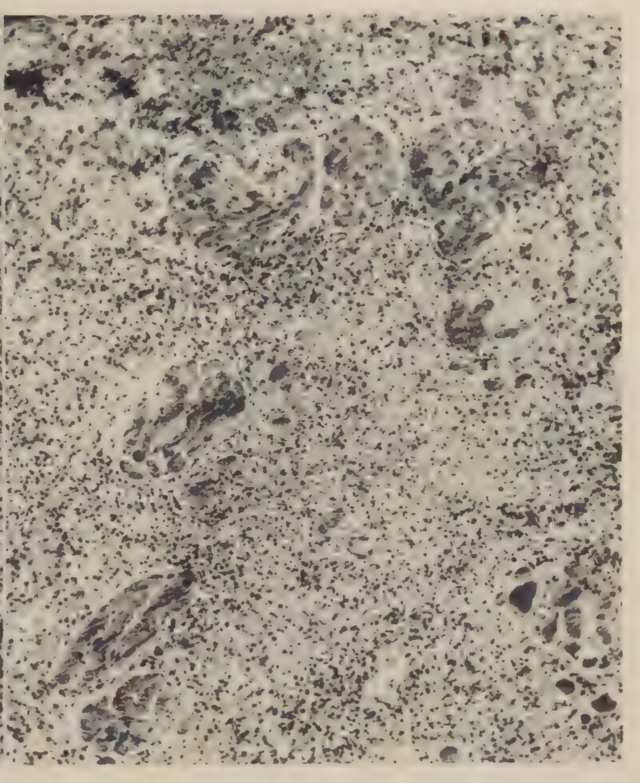
Acute inflammation that involved epiglottis, larynx, trachea, and bronchial tree in a 6 week old baby who had had a "cold" for a week and was found dead in bed several hours after feeding. **A.** Epiglottis: inflammatory exudate in edematous mucosa. x100. **B.** Vocal cord: prominent subglottic edema, congestion, scant exudate. x75. **C.** Trachea: active mucus production and exudate. x145.



Fulminant laryngotracheobronchitis in a 15 month old baby. Mild upper respiratory symptoms for a few hours, no fever, then sudden cyanosis and apnea. Small amount of bloody fluid drained from mouth during resuscitation efforts. **D.** Epiglottis: purulent, almost gangrenous mucosa. x55. **E.** Vocal cord: edema; hemorrhagic and purulent exudate; vessels engorged with leukocytes. x75. **F.** Trachea: mucopurulent exudate on surface; mucosal inflammation. x75.

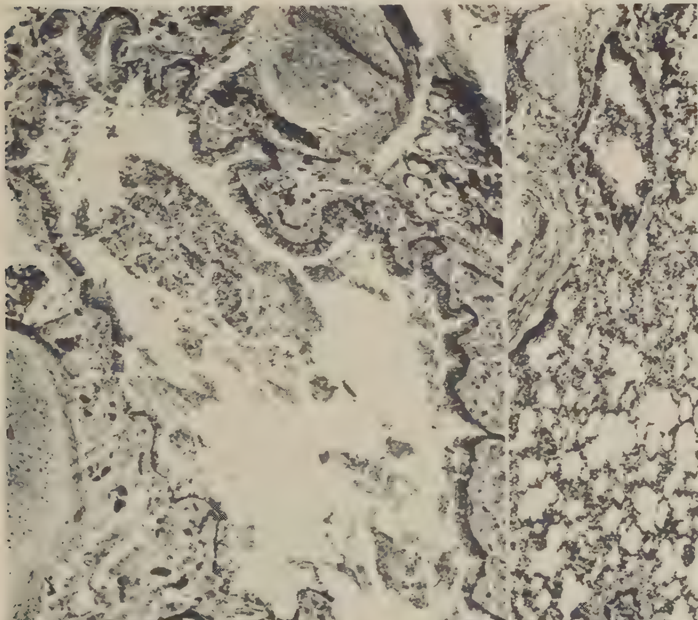


Mucosa of the laryngeal ventricle greatly thickened by edema and dense purulent exudate. x83.

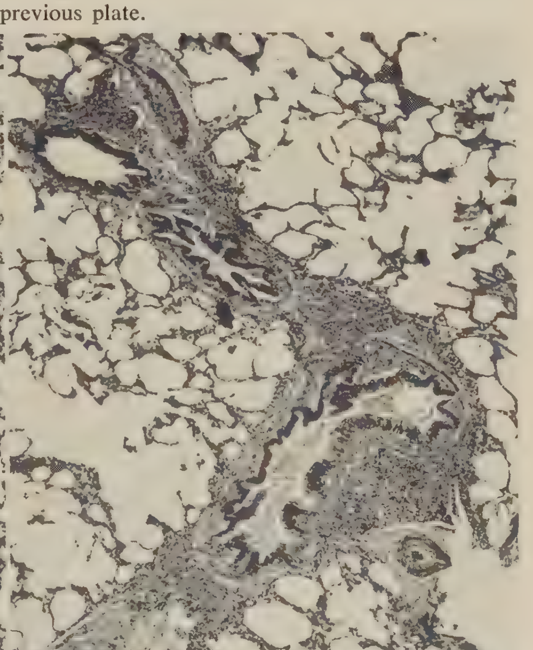


Thyroarytenoid muscle bundles are partly destroyed and widely separated by massive edema, suppuration and hemorrhage. x100.

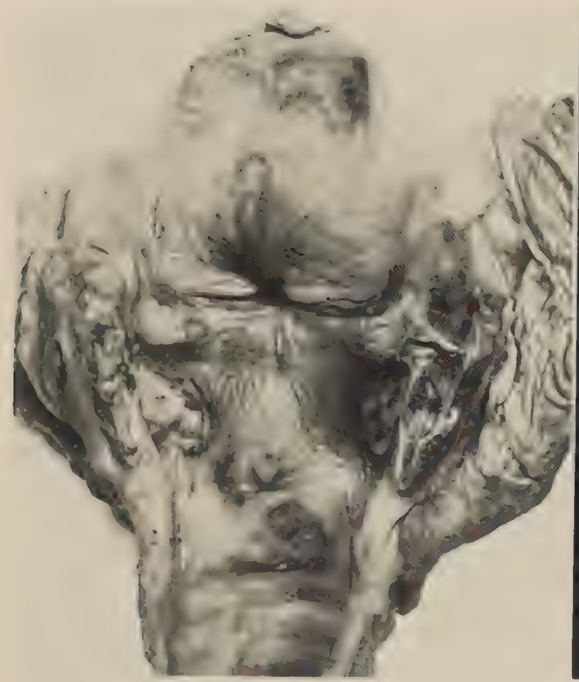
Both from case at bottom of previous plate.



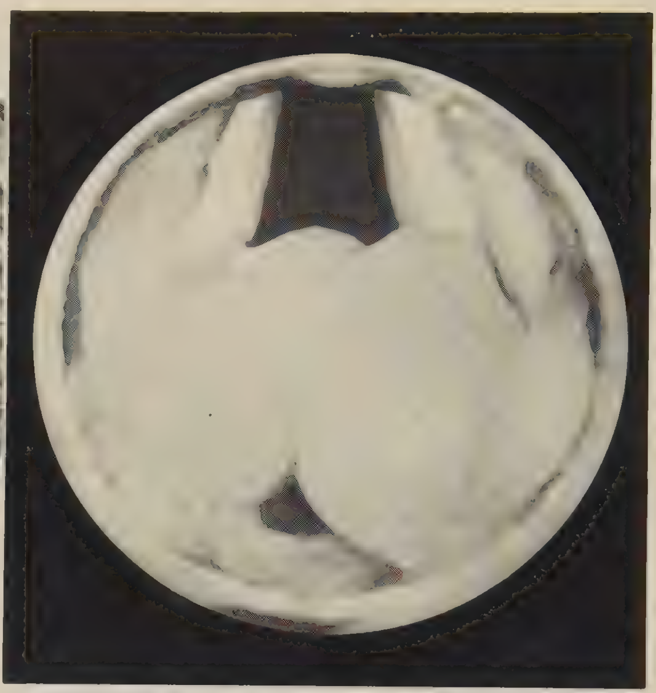
Bronchi in the same case. Congestion and partial epithelial desquamation of main bronchus *(left),* which contains inspissated, stringy exudate. Smaller bronchus and bronchiole *(center)* almost occluded by mucopurulent exudate. Both x48.



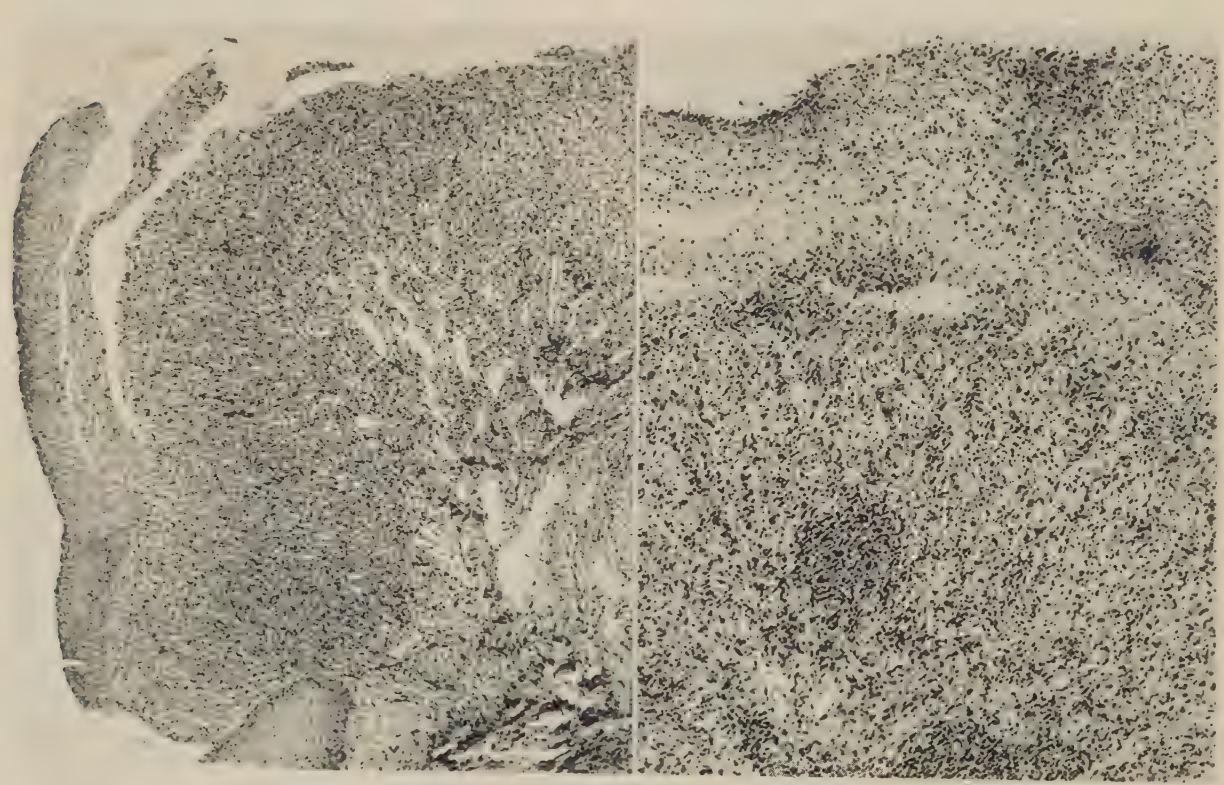
Postmortem pulmonary pathology commonly includes edema; atelectasis; emphysema *(shown above);* and lobular pneumonia. Sometimes an interstitial pneumonia, as in this case, is cause of delayed death. x48.



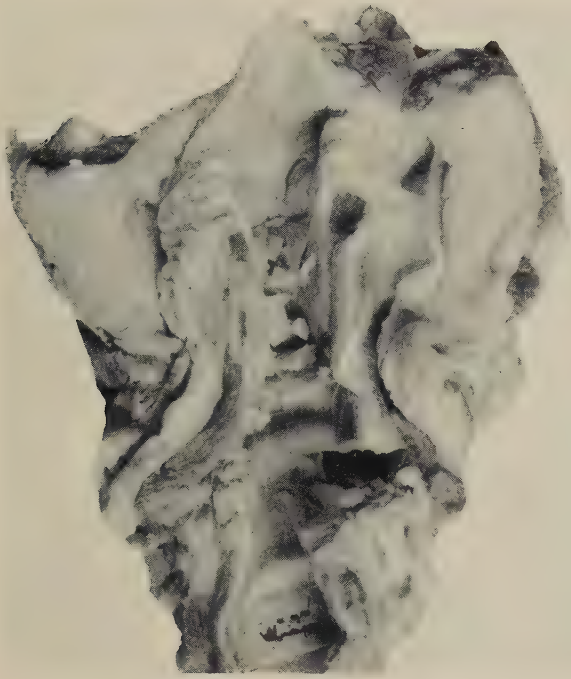
Ulcerations in posterior part of glottic region and in anterior subglottic mucosa following endotracheal anesthesia. (P. Holinger and E. Hirsch, Chicago, Ill.)



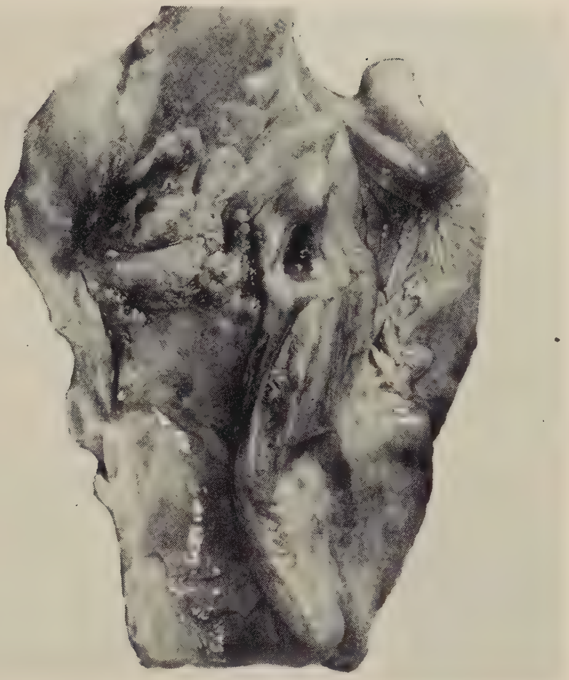
Edematous polypoid lesions over arytenoid cartilages and their vocal processes following intratracheal anesthesia. Direct laryngoscopic view. (P. Holinger.)



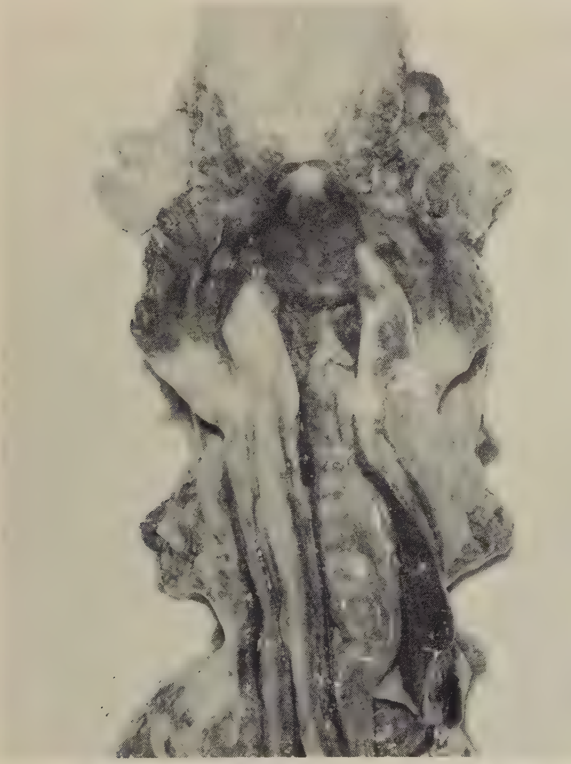
Granulation tissue polyp of posterior true vocal cord. From a 60 year old woman with hoarseness following endotracheal anesthesia several weeks previously. Newly formed capillaries with orientation perpendicular to the surface; proliferating fibrocytes; inflammatory exudate very dense because of surface ulceration. x55, x90. Though this is the most common postanesthetic laryngeal lesion seen by the pathologist, an occasional specimen may show fairly typical histologic features of granuloma pyogenicum.



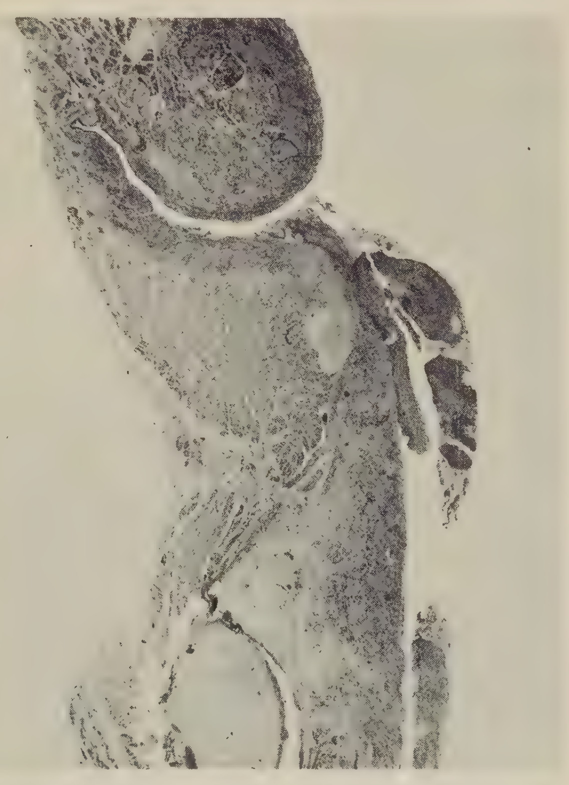
Remnants of diphtheritic membrane extending from vocal cords into trachea. 6 year old child with sore throat but no pharyngeal membrane. Death, two days after onset of illness, apparently due to asphyxia from aspirated fragments.



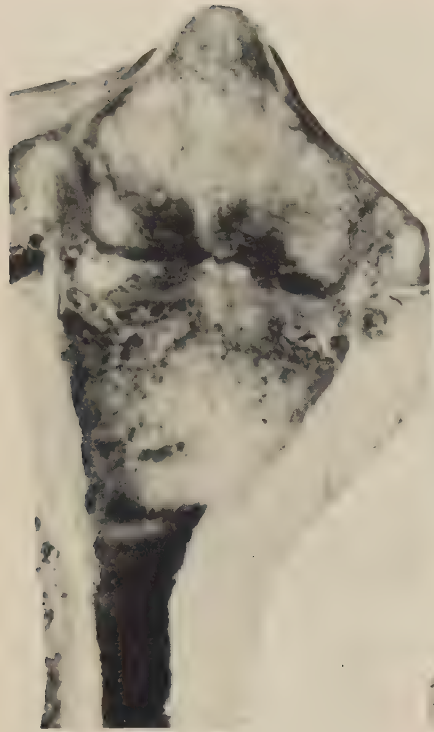
Laryngeal segment of complete pseudomembranous cast of entire laryngotracheobronchial tree from chronic alcoholic with undiagnosed illness for two weeks. Death with profound toxemia and bronchopneumonia.



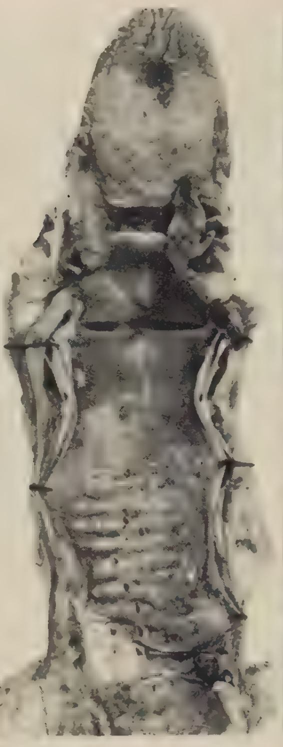
Cast of larynx and trachea formed by diphtheritic membrane that extended to bronchi. Edema, hyperemia, focal ulceration and necrosis of pharyngeal and lingual mucosa. Death from cardiac failure due to toxic myocarditis.



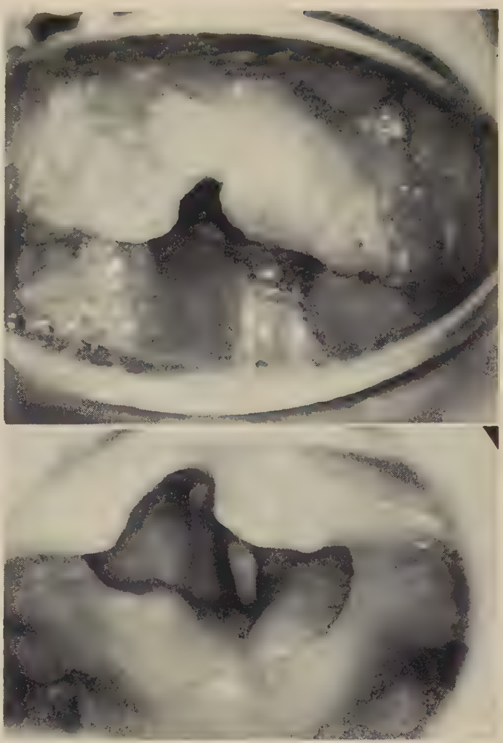
Fibrinous diphtheritic membrane, firmly adherent to partly necrotic true cord, more loosely attached to thickened subglottic mucosa. Longitudinal section of larynx of 3 year old child, ill four days before treatment. Tonsils and pharynx also involved.



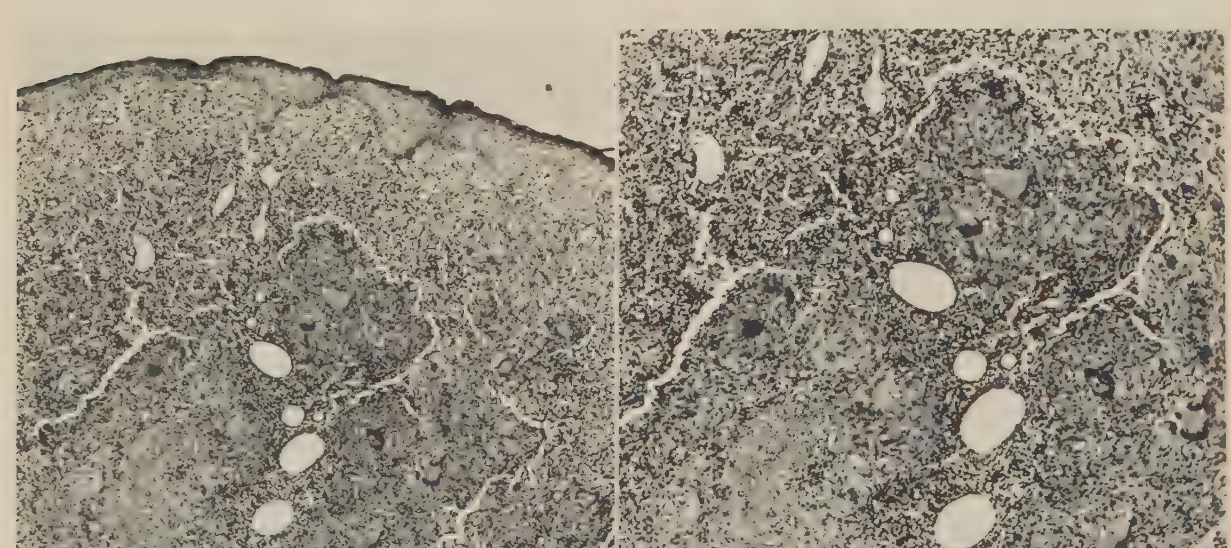
Extensive tuberculous laryngitis, secondary, as is usual, to pulmonary disease. Thickened, ragged, partly necrotic mucous membrane with superficial and deep ulcerations.



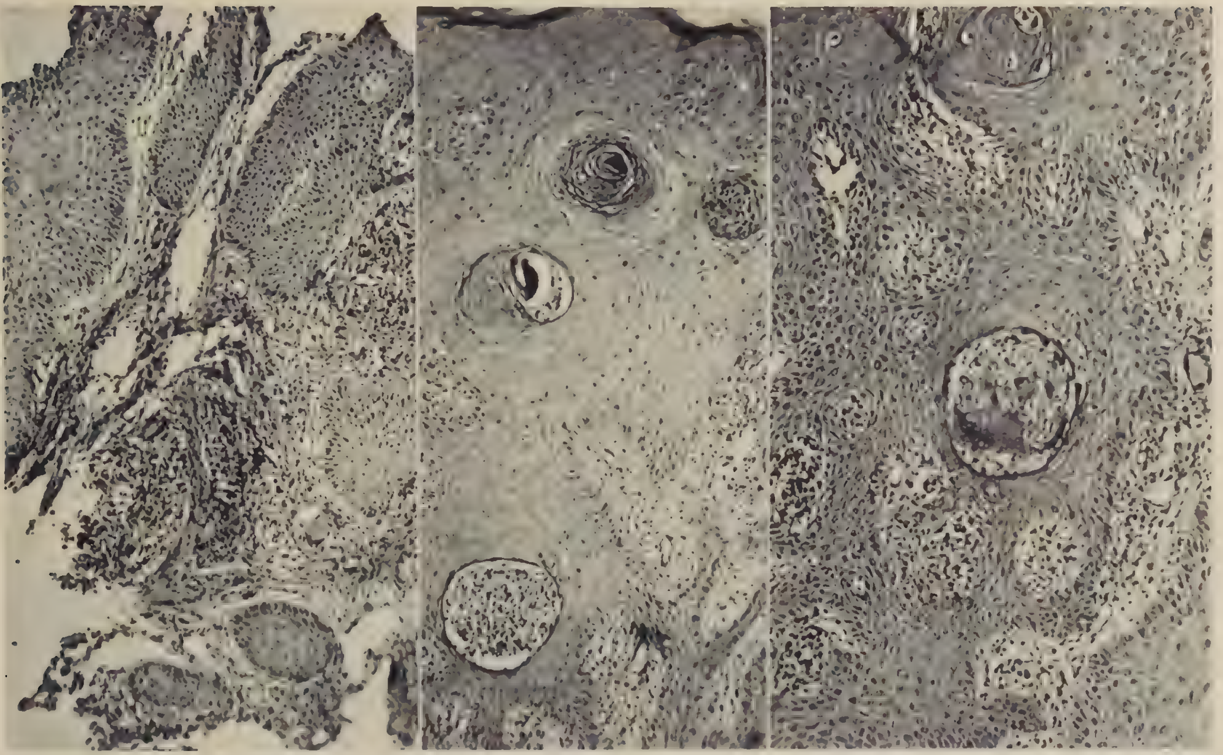
Tuberculous tracheitis. Mucosal infiltration and ulcers most severe between tracheal rings.



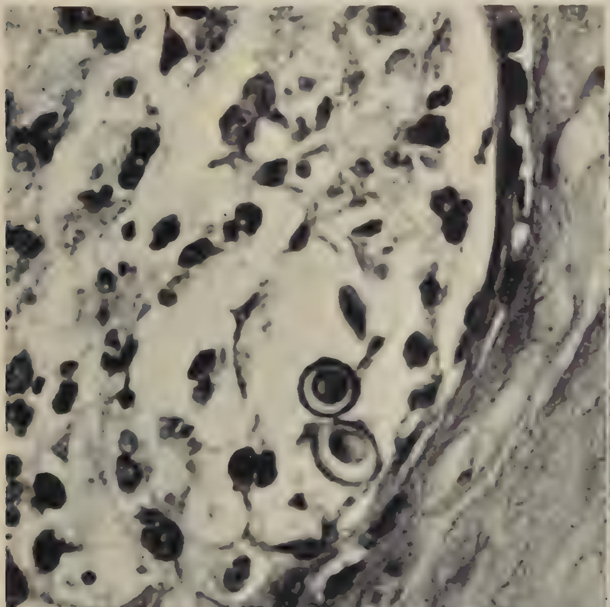
Before treatment *(upper),* extensive involvement of arytenoid area and epiglottis. Characteristic heart-shaped epiglottis.
After streptomycin therapy for six months *(lower).* (P. Holinger.)



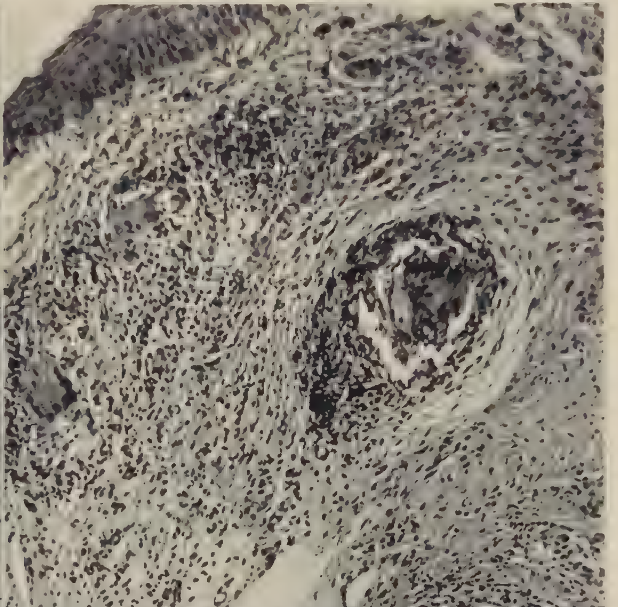
Diagnostic biopsy specimen from irregularly thickened vocal cord of adult with hoarseness for eight weeks. x48. Acid-fast organisms compatible with *M. tuberculosis* found in these tissue sections; confirmed by culture and guinea pig inoculation. Coalescent tubercles, some with central areas of caseation necrosis, in greatly thickened cordal mucosa. Numerous Langhans giant cells. x48, x75.



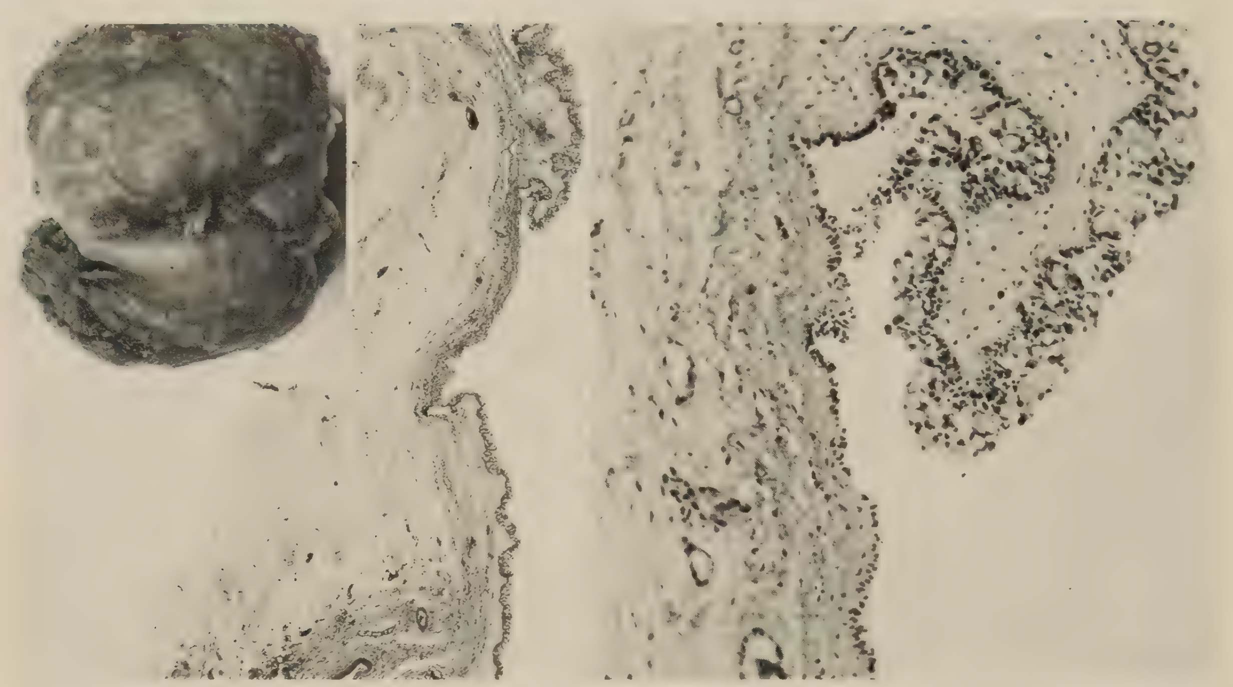
Blastomycosis of vocal cord. 65 year old farmer with persistent hoarseness, hospitalized for two years with diagnosis of "tuberculous laryngitis," transferred because carcinoma was suspected. Lungs clear. Marked pseudoepitheliomatous hyperplasia including pseudo pearl formation, simulating carcinoma *(left);* evidence of suppurative and granulomatous inflammation. Numerous intraepithelial microabscesses; occasional giant cells. x90, x100, x125.



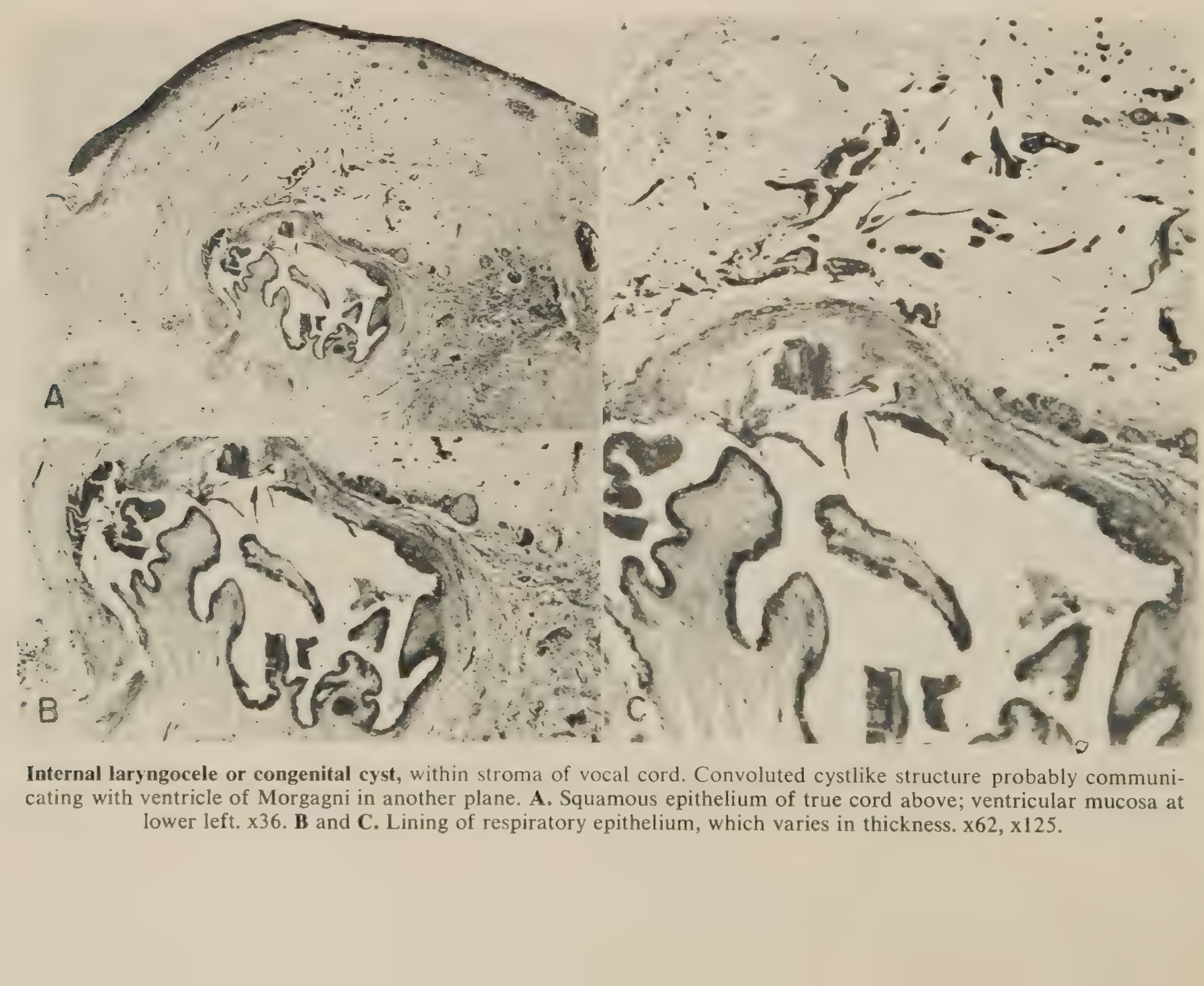
Typical spherical organisms with thick walls found within intraepithelial microabscess after repeated biopsy; surrounded by neutrophils, eosinophils, macrophages. x1125. *Blastomyces dermatitidis* cultured from several subsequent biopsies.



Discrete granuloma, originally interpreted as reaction to foreign body, and surrounding chronic inflammation and fibrosis were attributed to previous surgery and therapy in earlier biopsies. Review revealed occasional organisms in such lesions. x145.



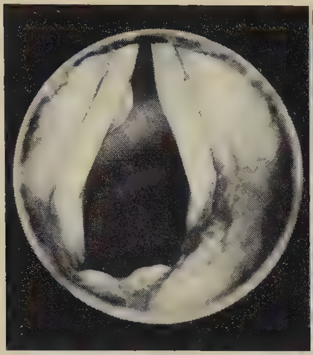
External laryngocele (diverticulum) in 38 year old man, present for many years as a soft swelling on left side of upper neck between the hyoid bone and superior border of the thyroid cartilage. It filled with air and bulged on coughing; was readily reduced by external pressure, producing a whistling sound. The thin-walled sac, a herniation of ventricular mucosa, is lined by partly desquamated respiratory epithelium. x23, x160. *Inset:* external laryngocele removed by external operation. (P. Holinger.)



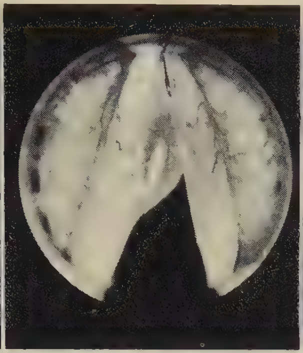
Internal laryngocele or congenital cyst, within stroma of vocal cord. Convoluted cystlike structure probably communicating with ventricle of Morgagni in another plane. **A.** Squamous epithelium of true cord above; ventricular mucosa at lower left. x36. **B** and **C.** Lining of respiratory epithelium, which varies in thickness. x62, x125.

THE LARYNGEAL NODULE

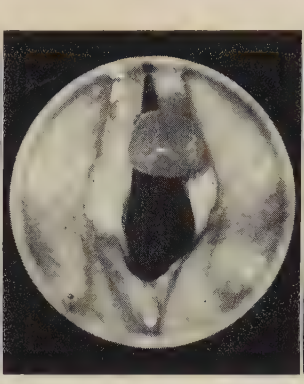
(VOCAL NODULE; SINGER'S NODE; NODULAR LARYNGITIS;
FIBROUS POLYP; EDEMATOUS POLYP; "AMYLOID TUMOR")



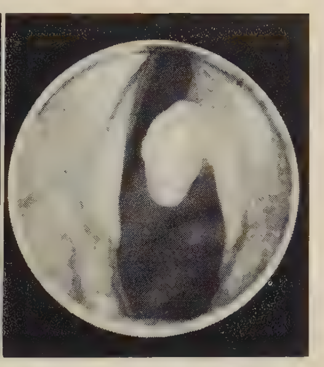
Sessile fibrous nodule on anterior left true cord.



Sessile edematous polyp in midportion of left cord.

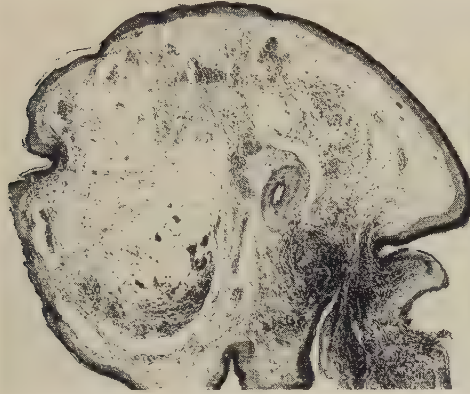


Pedunculated polyp of right cord. Edematous.

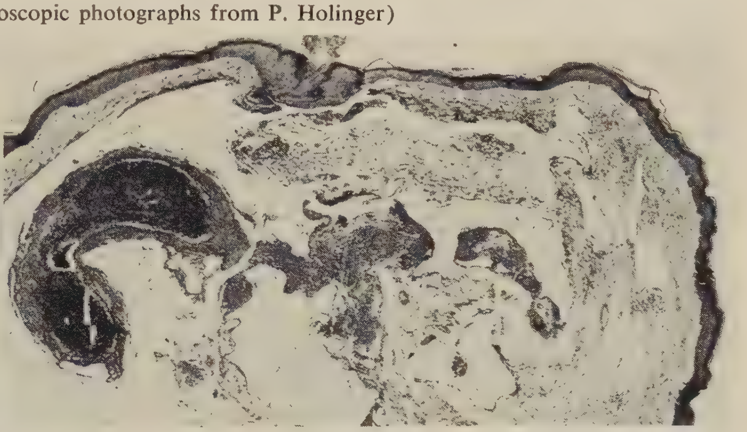


Pedunculated fibrous polyp on anterior right true cord.

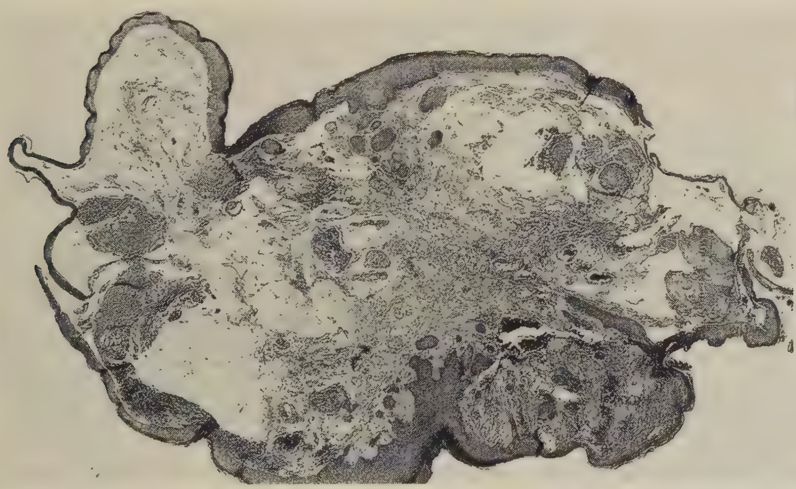
(Direct laryngoscopic photographs from P. Holinger)



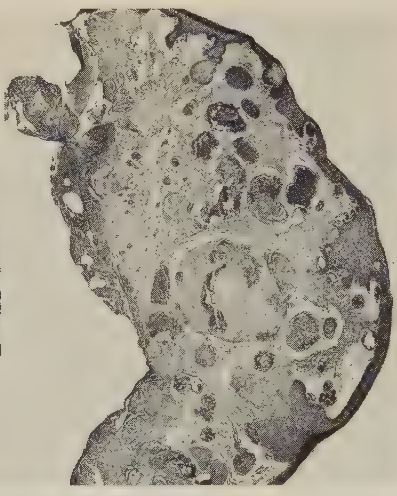
Edematous fibrous nodule. Pedunculated mass on left cord had "venous blue color" due to dense hemosiderin pigment. 26 year old man, hoarse for eleven months. x24.



"Varix" or vascular node. Numerous dilated thin-walled vessels; edematous stroma with focal hyalinization. Masses of fibrinoid material within and around vessel walls. x28. "Laryngeal polyp" previously removed from 42 year old man. Recurrent hoarseness for one year.

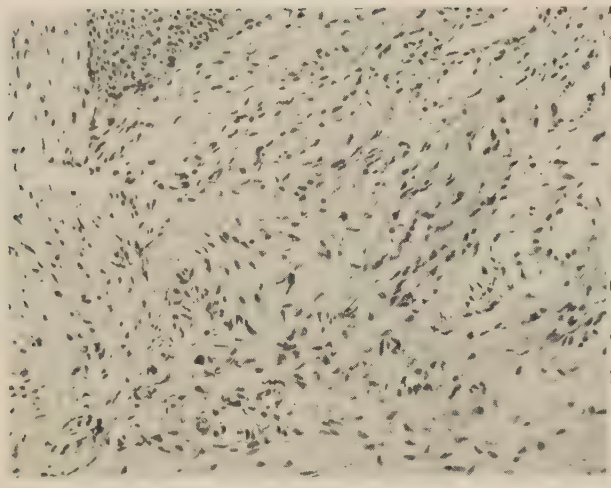


Nodule with mixed stromal features. Partly edematous, partly hyalinized stroma; hyalinizing fibrinoid material. x9. Patient hoarse for two years.

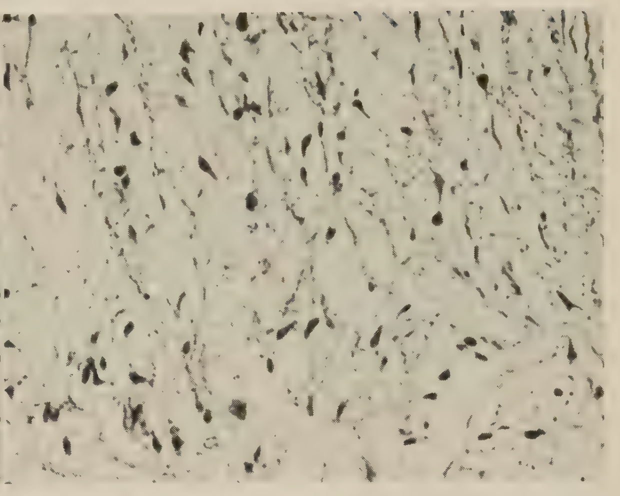


Hyaline stage—often erroneously termed "amyloid tumor." x21.

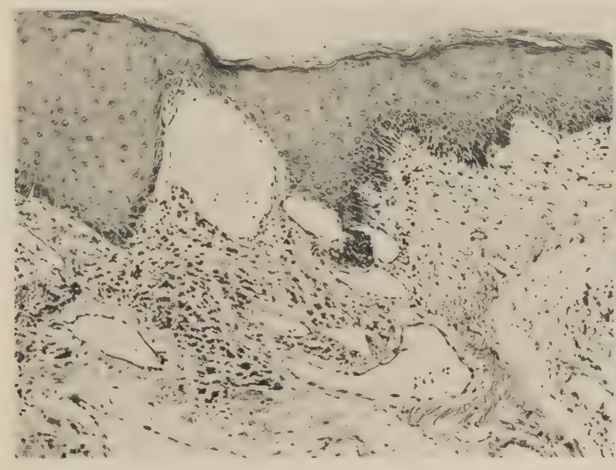
The squamous epithelium covering laryngeal nodules may be similar to that of the adjacent normal vocal cord epithelium; more frequently is somewhat atrophic or acanthotic; occasionally shows marked focal hyperplasia and keratosis or pronounced pseudoepitheliomatous hyperplasia, as in last two figures.



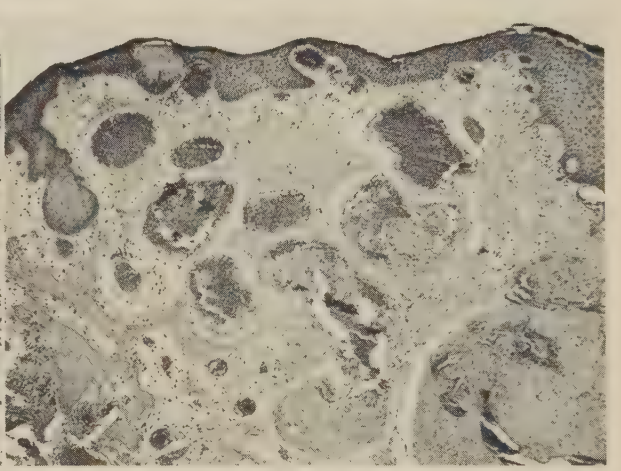
Fibrous nodule ("first stage"). Small node with cellular, rather dense connective tissue. x125.



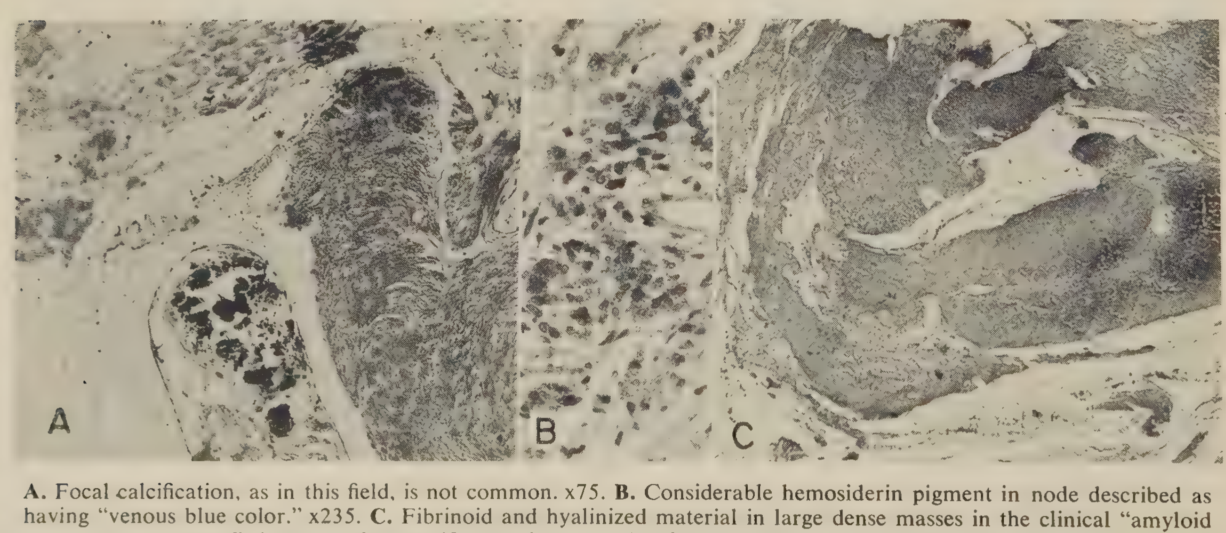
Edematous nodule ("second stage"). Fibrils separated by edema produce myxomatous appearance. x210.



Vascular nodule ("third or varix stage"). Numerous greatly dilated vessels with walls practically limited to an endothelial lining. x48.



Hyaline (fibrinoid) "fourth stage." Masses of pink-staining material in stroma and in obliterated vessels and their walls. From patient hoarse for five years. x30.



A. Focal calcification, as in this field, is not common. x75. **B.** Considerable hemosiderin pigment in node described as having "venous blue color." x235. **C.** Fibrinoid and hyalinized material in large dense masses in the clinical "amyloid tumor" does not give specific reaction to stains for amyloid. Crystal violet stain. x50.

CHAPTER 25

TUMORS OF THE LARYNX

Two kinds of **cysts** are occasionally encountered in the epiglottis and laryngeal mucosa. The commoner is the retention cyst resulting from occlusion of a gland duct. The contents are mucoid and the cells by which it is lined, cuboidal. The other kind is an embryonal inclusion of respiratory epithelium. The epithelium is usually columnar and cilia can occasionally be identified. The inclusion can be of branchial-cleft epithelium, in which case the cyst will be lined by squamous or columnar epithelium with an associated lymphatic tissue element.

Papilloma of the larynx is of two clinical categories, depending on whether it occurs in the young or in the adult. There is, however, no difference histologically. The papilloma occurs more frequently in children than in adults and usually manifests itself in the first few years of life. It is more common on the anterior third of the vocal cord or in the commissure, but it is not necessarily restricted to the cord. It shows a persistent tendency to recur after removal, and there is a possibility that it can be implanted in other portions of the larynx from the primary tumor. This is interpreted as evidence that the tumor is of viral origin. With the onset of puberty the lesion tends to regress spontaneously. This characteristic, in turn, has been attributed to hormonal influence, especially of estrogen. The tumor is not malignant, but it may cause death from sudden congestion or by exciting glottic edema. The importance of progressive hoarseness has been emphasized as an indication for direct laryngoscopic examination to determine whether papillomatosis is the cause.

Papilloma in the adult, while usually benign, does not show the tendency to regression of the juvenile papilloma. It is more frequently a single lesion than it is in children. It occasionally undergoes degeneration into squamous cell carcinoma, particularly after repeated partial removals. Jackson and Jackson reported a 3 per cent incidence in their 205 cases. On the other hand, Holinger and coworkers had none that were malignant among their 109 cases.

The pathologic picture of this lesion is identical with squamous cell papilloma in other regions. It is either sessile or pedunculated. The latter form consists of delicate vascularized fingers of connective tissue stroma covered by layers of squamous epithelium with a normal regular basal cell layer, broad squamous cell layer, and either a parakeratotic or a keratotic surface. The keratotic surface is usually seen in adult tumors. The cells generally are regular in size and arrangement and mitotic figures are scarce, if present at all. There is usually a chronic inflammatory reaction in the stroma of the villae or of the mucosa. Generally the epithelium of the adjacent mucosa is thicker than normal.

The sessile type is difficult to differentiate from inflammatory hyperplasias of the mucosa. It may consist of a few peg-like projections above the surface level.

Indications of impending or actual malignancy are the presence of dyskeratotic cells in the prickle-cell layer, a loss of polarity in the basal cells, the presence of mitotic figures, particularly atypical ones, and the infiltration of the epithelium into the stroma.

Benign adenoma of the larynx is rare and consists of a mass of well differentiated mucus-gland acini. The bronchial type of adenoma discussed in the section on the lungs is occasionally found in the mucosa of the larynx.

Lipoma, made up of mature fat tissue, occasionally develops in the larynx.

As part of a general **xanthomatosis** the laryngeal mucosa may contain collections of lipoid-containing histiocytes. They will be evident clinically as small yellow masses scattered in the mucosa, or as larger tumors. The presence of similar tumors of the skin will indicate the true nature of those in the larynx.

Fibroma is rare in the larynx. It is more common in the male adult and may be on an inflammatory basis. It arises most frequently from the false cord and from the wall near the commissure. It is usually pedunculated and may attain a surprisingly large size. One laryngeal fibroma in the Registry was from a 50-year-old man who had been hoarse for several months. He died suddenly from asphyxiation. In spite of the disturbing histologic character and size of the tumor, it had not metastasized.

Histologically, the fibroma is very cellular and there may be sufficient pleomorphism of the cells to warrant a histologic diagnosis of sarcoma. From experience with the Registry material, however, it seems that despite this alarming histologic picture it is usually not malignant clinically, and complete removal without radical procedures and without irradiation treatment usually suffices for a cure. The tumor, however, is not always benign. It can invade the laryngeal wall and metastasize to the regional lymph nodes.

An important point to remember in connection with these pedunculated laryngeal tumors is that they are usually complicated by profound changes in the epithelium that may involve the entire mucosa, including the glands, in metaplasia toward the squamous. This altered epithelium can then undergo malignant dyskeratosis with the final result of frank squamous cell carcinoma. This is well illustrated by two cases shown in the following plates. Both patients were adult white males who had had pedunculated tumors hanging into glottis and larynx for some time. On final examination of these tumors and larynxes, both of the former proved to be histologically malignant mesenchymal tumors. In one, the epithelium of the entire larynx, including the ventricles and the mucous glands, had undergone squamatoid metaplasia with some dyskeratosis but no actual invasion, a picture resembling that seen in epidermization of the cervix. In the other case, the epithelium which had undergone metaplasia showed generally the leukoplakic type of dyskeratosis, and frank squamous cell carcinoma already had invaded the original tumor, an example of "colliding tumors." It is this phenomenon that probably accounts for the reports of so-called carcinosarcoma in the larynx.

Chondroma of the larynx is rare. It is not an uncommon experience to find elastic cartilage in material removed from the larynx for other conditions, especially in tissue from the commissure and arytenoid cartilages. This may be mistaken for tumor. The cartilages of the larynx seem to undergo nonneoplastic proliferation as a result of chronic inflammation. True tumors do occur, however, arising most commonly from the thyroid and the arytenoid cartilages. One that developed in the true cord of a 66-year-old man is illustrated in the plates.

An example of a congenital chondroma of the cricoid cartilage was received in the Registry recently. The tumor grew rapidly and compromised the laryngeal lumen to the extent of causing massive atelectasis of the lungs. The esophagus was also constricted. The baby died at two months of age.

The Registry has no record of a CHONDROSARCOMA of the larynx.

Tumors of nerve origin are rare. An example of a **neuroma** made up of myelinated nerve fibers is illustrated.

Myoblastoma. – The larynx is one of the more common sites of myoblastoma. It occurs especially in the vocal cords and usually in relationship with striped muscle elements. This tumor is discussed in more detail under general tumors.

Rhabdomyoma is very rare in the larynx, although Gluck reported a laryngeal tumor diagnosed rhabdomyomyxosarcoma in a 10-year-old child. It was a pedunculated tumor attached to the left cord, and removal was accomplished by snare and subsequent laryngofissure. There was no recurrence after four years. This case is also included in the illustrations.

Angioma. – Moore reviewed 70 cases from the literature, but judging from the descriptions and locations, the majority probably represented the varix stage of the laryngeal nodule. He observed that lymphangiomas are very rare. He reported that hemoptysis is not common but that bleeding at operation can be very troublesome.

Hemangioma.–Sweetser reported a hemangioma in a baby who died about two months after birth following a series of attacks of sinus and cardiac difficulties. At autopsy there was a diffuse, flattened, grayish-purple bulging of the mucous membrane within the circle of the cricoid cartilage, several millimeters below the cords. It occupied the entire circumference of the larynx except at the posterior commissure. Microscopically, the swelling was found to be a mixture of large and small blood channels, some of them cavernous, with a delicate stroma. No other hemangiomas were discovered.

Hemangiomas that have been reported have occurred most commonly in patients more than 20 years of age, twice as frequently in males. They are usually sharply demarcated. They may be situated below the true cords but the greater number are attached either to or are above the cords. They probably belong to the group of congenital tumors.

The student is referred to the article by New and Erich for a comprehensive review of benign tumors of the larynx and to the more recent one by Holinger and Johnston on the same subject.

CARCINOMA OF THE LARYNX

Carcinoma is the commonest malignant tumor of the larynx. It is a tumor of adult life and is seen overwhelmingly in the male, rarely in the female. The youngest patient in the Registry group was 25 years of age. Carcinoma in the larynx is practically always of the squamous cell type, although an occasional one may retain the basal cell character. Of 76 cases in the Registry, only one was of the basal cell type. It occurred in a woman who had local symptoms for 12 years. Adenocarcinoma is even more rare.

Carcinoma may arise on the basis of a long-standing papilloma or more commonly from leukoplakia. Depending on location, the tumors can be divided into two groups, the INTRINSIC, which occur within the larynx, usually having origin on the cords; and the EXTRINSIC, which arise from the arytenoid cartilages, the epiglottis, in the pyriform fossae and in contiguous portions of the tongue and hypopharynx.

Intrinsic cancer is essentially a tumor of the male, and Holinger reported that in his experience only 10 per cent occurred in women. Extrinsic cancer is even rarer in the female. Hoarseness is always a symptom in intrinsic carcinoma, while dysphagia is a common early symptom in the extrinsic, but is absent in the purely intrinsic.

The clinical courses of the two are quite different. The intrinsic cancer tends to be slow-growing, non-aggressive, highly differentiated, and late in metastasizing. The extrinsic cancer, on the other hand, grows more aggressively, metastasizes earlier, and its cells do not exhibit the high degree of differentiation usually seen in the intrinsic tumor. Another detrimental feature of carcinoma of the larynx, especially the extrinsic, is that metastasis is primarily to the deep-lying nodes along the internal jugular veins. Formerly, the prognosis of extrinsic laryngeal carcinoma was regarded as almost hopeless, but bold and skillful modern surgery has resulted in five-year cures in as much as 25 per cent of some series. Fortunately, the extrinsic is far less common than the intrinsic form.

Intrinsic cancer is predominantly a tumor of the anterior portion of the cords and ventricles, the majority situated on the anterior portions of the cords. The anatomic basis for slow metastasis from this area has been mentioned under the histology of the cord. If the cord becomes fixed it means that there has been penetration of the barrier around Reinke's space and that dangerous infiltration has occurred. In advanced cases there may be extension of the tumor from one area to another so that it will lose its clinical identity as intrinsic or extrinsic.

Grossly, the intrinsic tumor may be papillary and associated with frank thickening of the adjacent mucosa, or it may be a more diffuse swelling with a smooth surface. In either case, it is in only the later stages that there is frank ulceration. A specimen of tissue carefuly selected to include obvious tumor and neighboring uninvolved mucosa should be taken for examination if there is any uncertainty concerning the nature of the lesion.

Microscopically, the tumor does not differ from epidermoid carcinomas of other parts. Nests and strands of epithelium exhibiting more or less squamous differentiation and including epithelial pearls characterize the tumor. The widely infiltrating tumor of long standing shows less differentiation, and from the examination of a few groups of cells it may be difficult to identify the extrinsic tumor as carcinoma because of its anaplastic spindle-cell character.

The **transitional cell carcinoma** of the type that is so common in the upper respiratory tract does not develop in the larynx, although there is a possibility that the extrinsic tumor may be of that type.

Sarcoma of the larynx is very rare and is usually of fibrous origin, although instances of lymphosarcoma are reported.

Tumors primary in the epiglottis are unusual, but among the following illustrations are congenital cysts, bronchial adenoma, and nevus.

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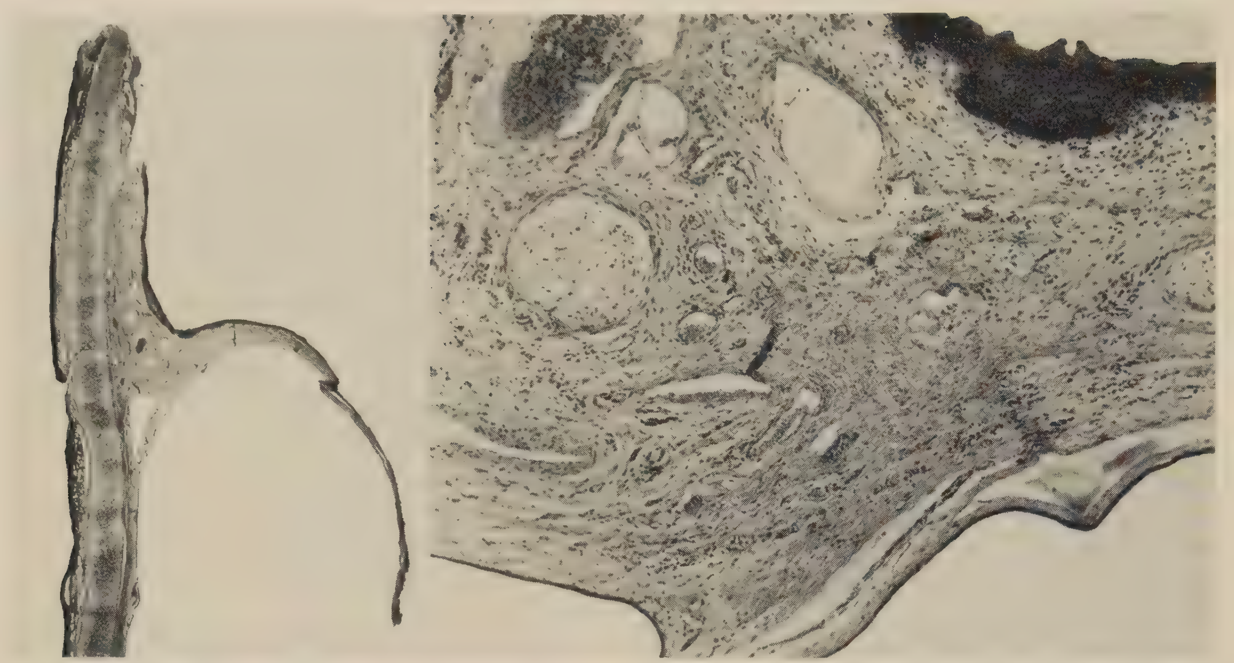
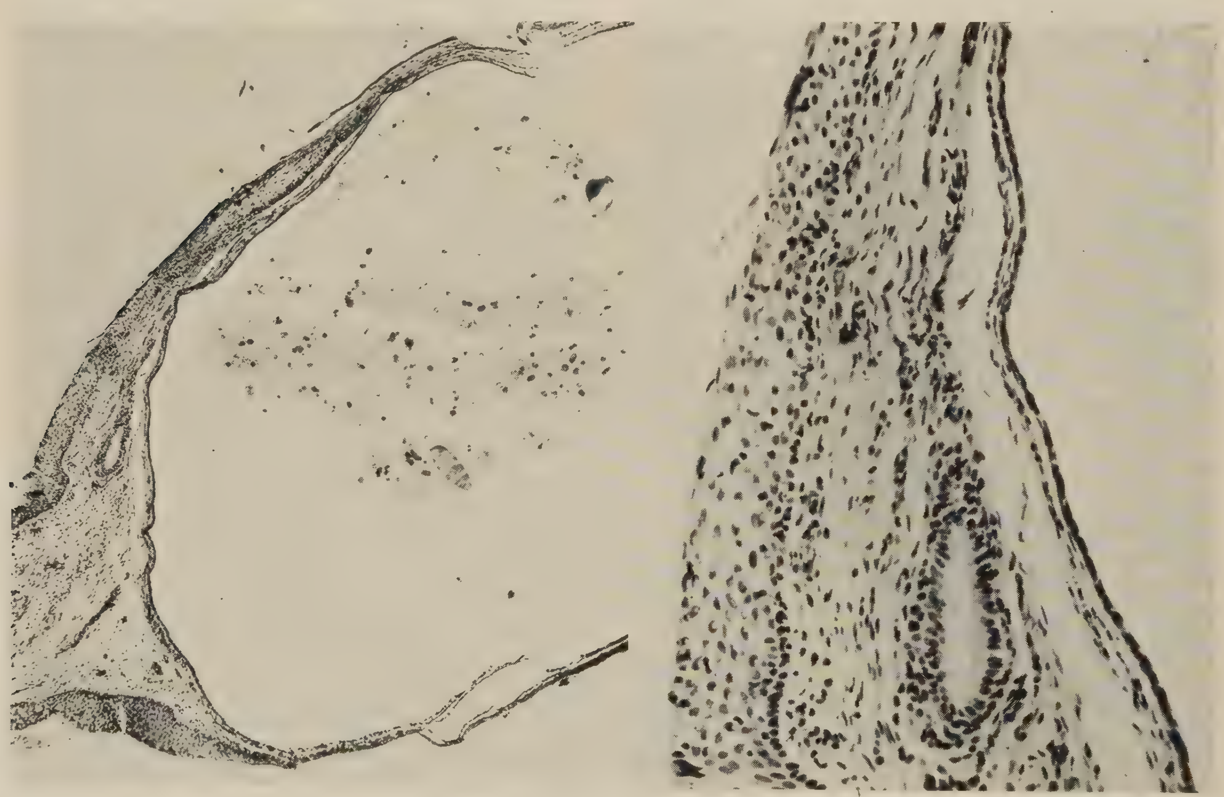
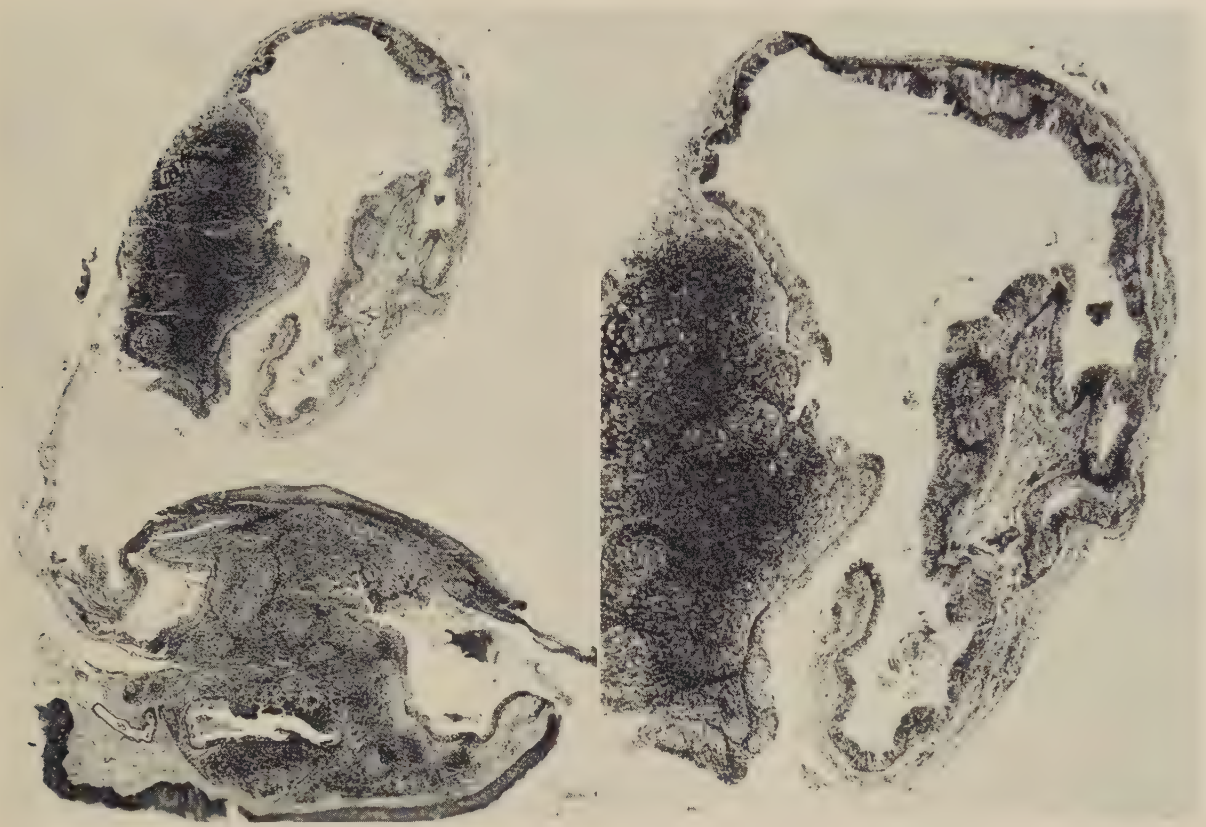


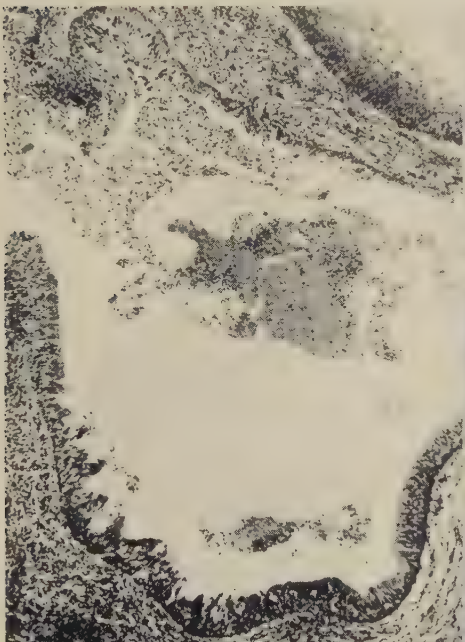
Retention cyst, lingual surface of epiglottis, manifest as smooth mass in vallecula that extended into soft tissues of preepiglottic space below. From 40 year old man with sensation of "a splinter in the throat" for several years. *Left:* epiglottis with large cyst, and a small accessory cyst on lingual surface. Note firmly attached mucosa of laryngeal surface. x5. *Right:* wall of cyst, at bottom, is composed of a single layer of flattened cuboidal epithelium surrounded by dense fibrous tissue. Squamous epithelium of epiglottic mucosa above. x90. (S.S. Hall, Clarksburg, W.Va.)



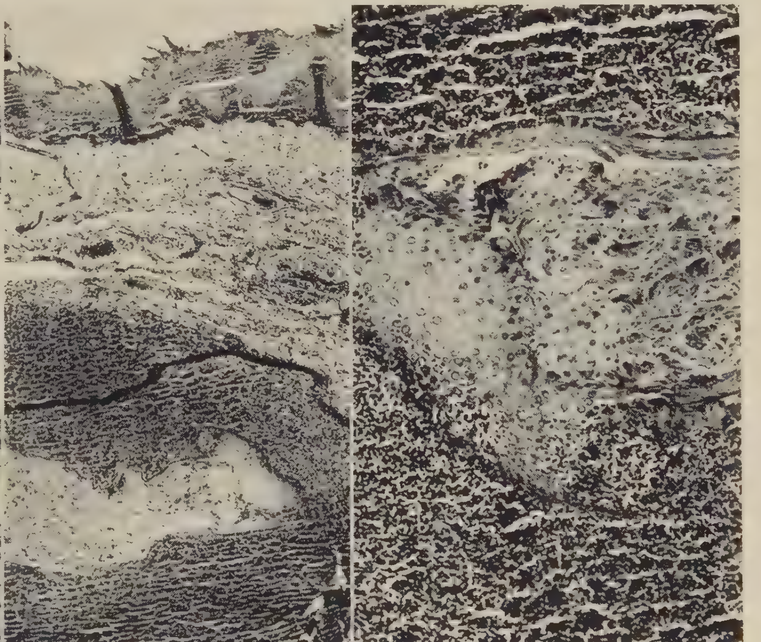
Retention cyst, left arytenoid, presented as a "laryngeal tumor" adjacent to posterior end of left true cord in 54 year old woman with hoarseness for several years. Large cyst contains inspissated mucus and is lined by one or two rows of flattened cuboidal cells. Stratified squamous epithelium of arytenoid mucosa at left. x48, x180.



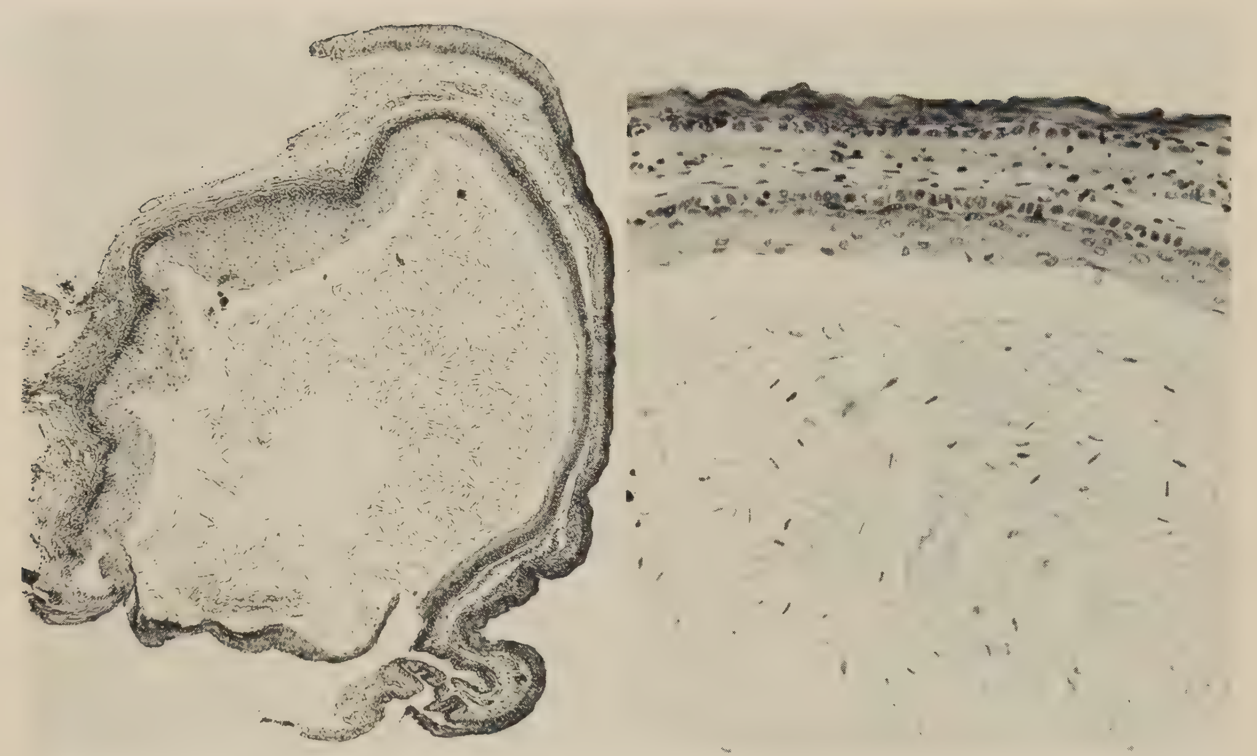
Multiple cysts of branchiogenic origin from pyriform fossa and epiglottis of 66 year old man complaining of hoarseness. Lymphoid tissue surrounds cysts, which are lined largely by hyperplastic pseudostratified columnar epithelium, parts of which show dense lymphocytic infiltration. x20, x33. (A.O. Severance, San Antonio, Tex.)



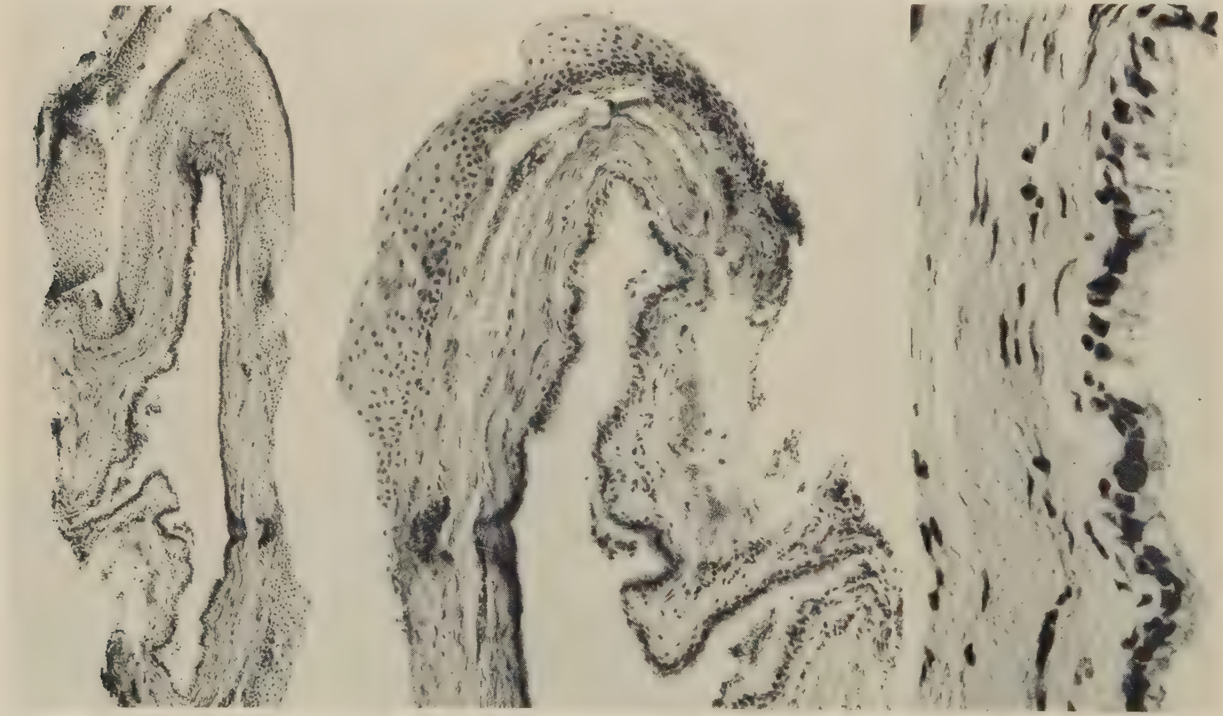
Respiratory epithelium, partly ciliated, of superficial cyst. Stratified squamous epithelium of hypopharyngeal surface at upper right. x60.



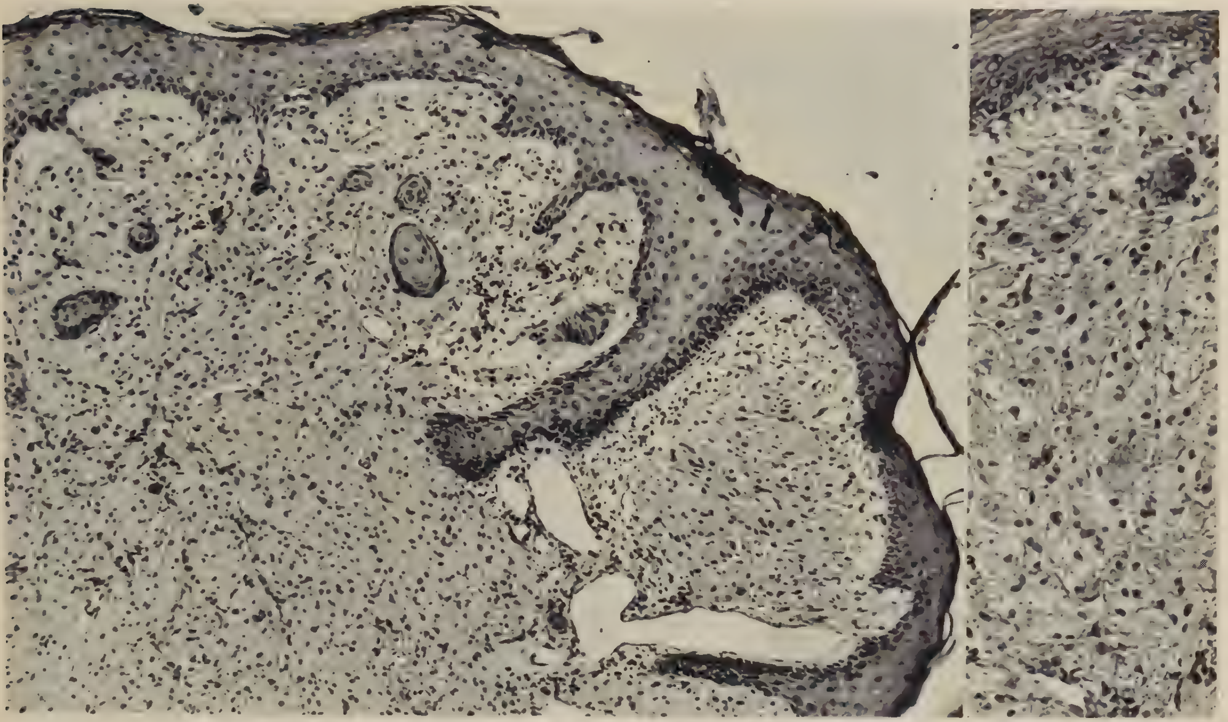
Branchiogenic remnants within essentially normal pharyngeal mucosa resected with larynx. Nest of orderly keratinizing squamous epithelium within circumscribed mass of dense lymphoid tissue. Surface epithelium of pharynx at upper left. x32, x113.



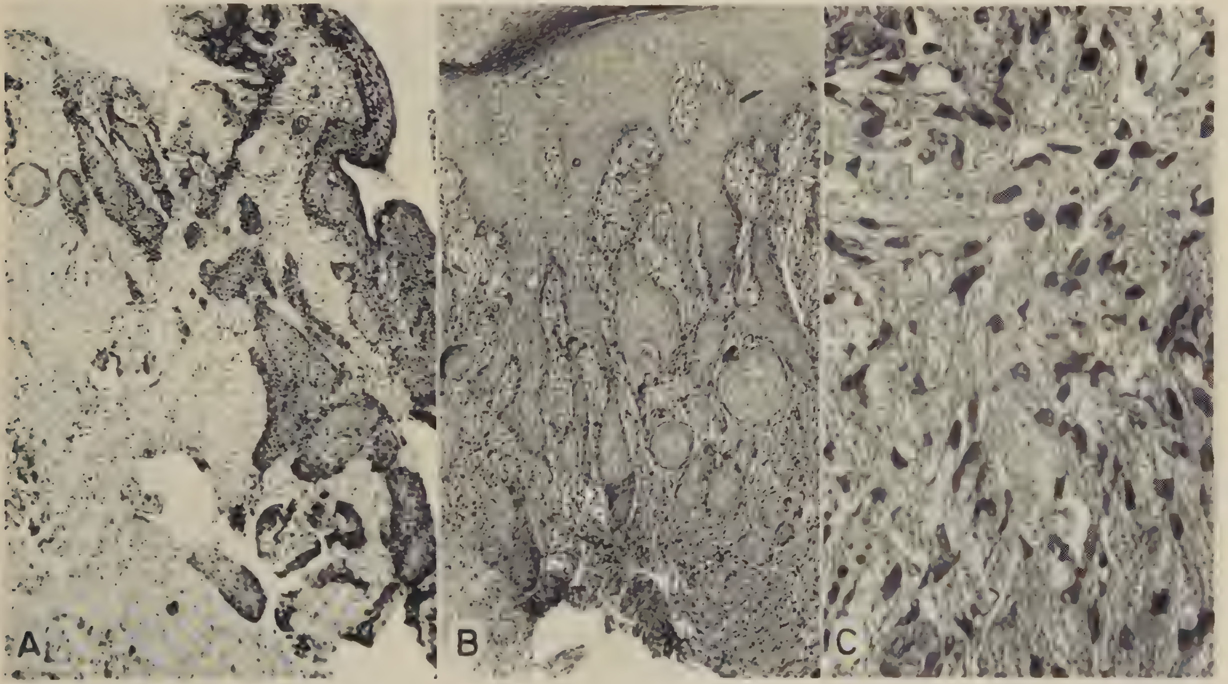
Epidermoid inclusion cyst, of possible traumatic origin, within true vocal cord of 21 year old man with hoarseness. *Left:* free edge of vocal cord at right. x41. *Right:* cyst is lined by squamous epithelium and filled with parakeratotic cells and keratin. Moderately atrophic squamous epithelium of cord above. x165.



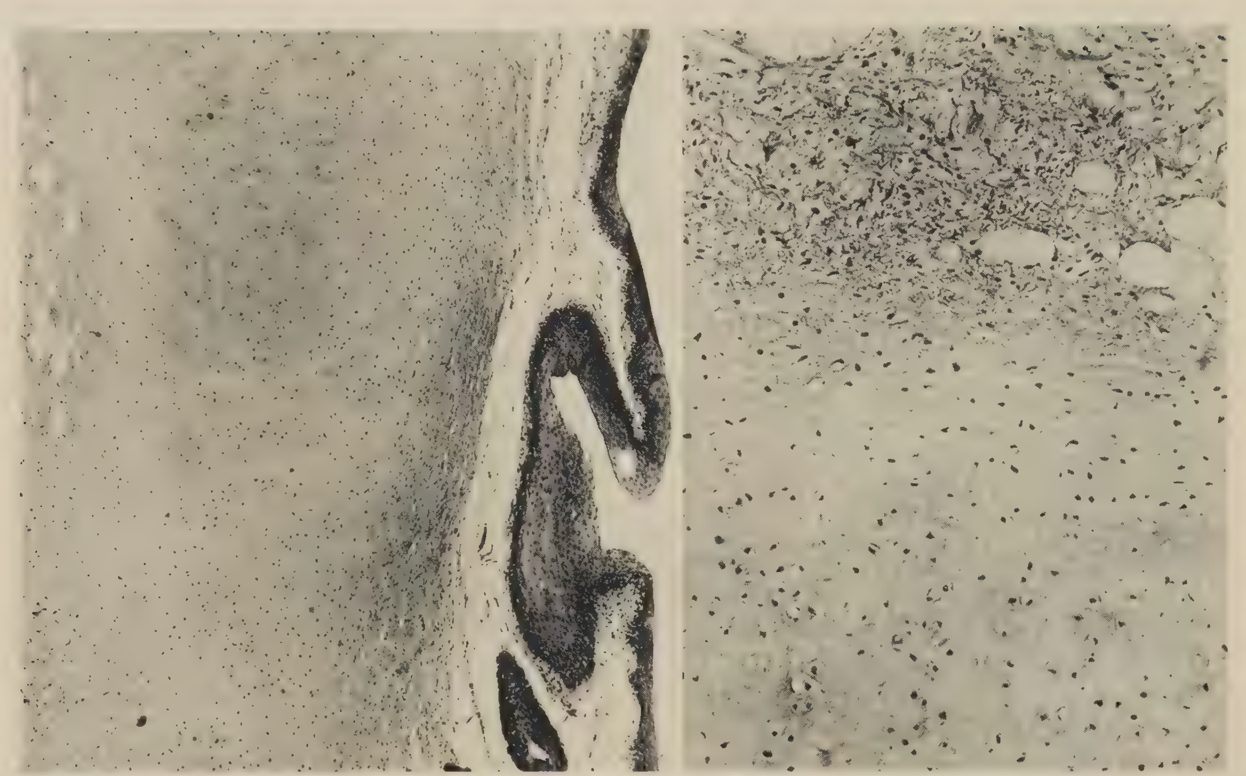
Mucous retention cyst, lined by cuboidal and columnar mucus-secreting epithelium, had expanded free edge of vocal fold and extended "somewhat subglottically." A 19 year old man with recurrent laryngitis for two years. x48, x125, x400. Since the normal true cord contains no glands, such a cyst usually arises from an occluded duct of adjacent subglottic glands, and extends into the loose subepithelial tissue of the vocal fold as it enlarges, due to the pressure of accumulating secretion.



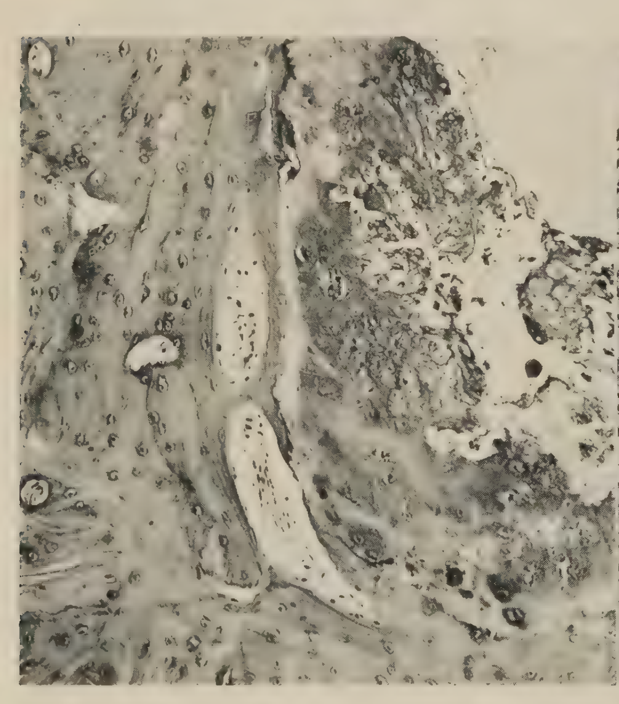
Granular cell myoblastoma, a tumor of controversial histogenesis. Some favor a myogenic, neurogenic or fibroblastic origin; others believe they are inflammatory or degenerative lesions, not neoplasms. Typical polypoid mass from vocal cord of young woman. Poorly defined or rounded cells with granular eosinophilic cytoplasm and dark centrally placed nuclei. Hyperplasia of overlying epithelium is a frequent feature. x83, x150.



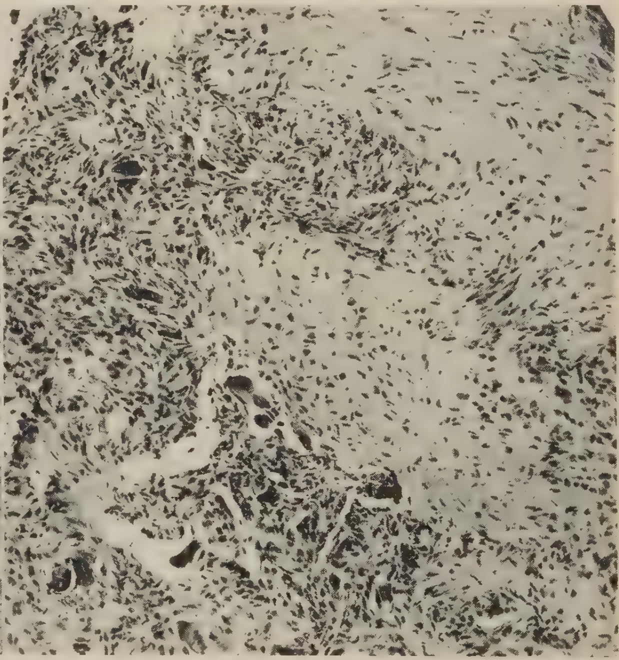
Pseudoepitheliomatous hyperplasia may be pronounced in laryngeal lesions, and superficial biopsies are not uncommonly misdiagnosed. **A.** Mass over vocal process of arytenoid, diagnosed papilloma or early invasive carcinoma, from 41 year old woman with hoarseness. x45. **B** and **C.** Fungating lesion on left cord from 24 year old man, previously treated for syphilis and hoarse for two years. Granuloma or malignant tumor suspected. The underlying myoblastoma (**C**, x395) was obscured because of the predominant epithelial element and very scant stroma included in the superficial biopsy, the entire thickness of which is shown in **B**, x55.



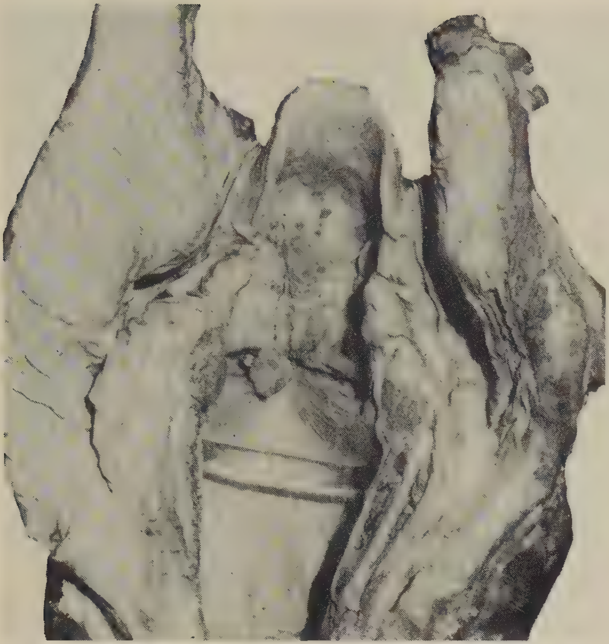
Chondroma of posterior true cord presented as firm swelling causing marked narrowing of glottis of a 66 year old man with dysphagia. Carcinoma suspected; coronary death four days after laryngectomy. Well differentiated cartilaginous neoplasm with evidence of active proliferation in some foci. x48, x90. (R.T. Smith, Fort Smith, Ark.)



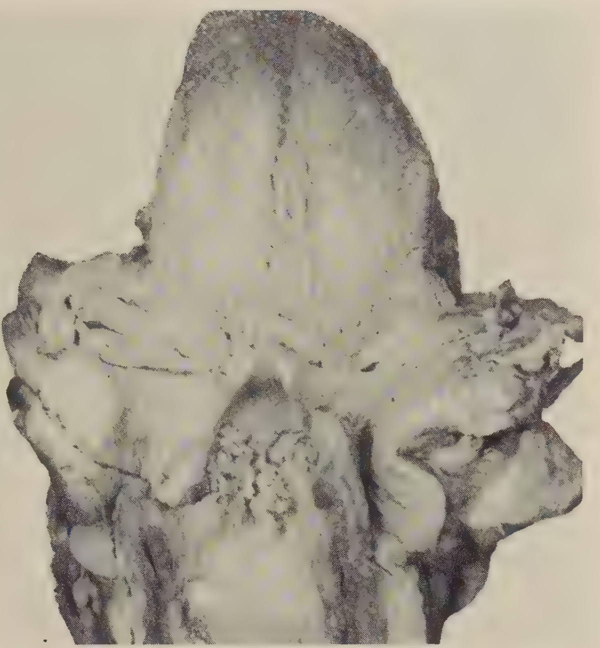
Osteochondroma projecting from posterior surface of the larynx at the level of the cricoid cartilage, caused progressive hoarseness and immobilization of cords for three years in a 71 year old man. Irregular masses of cartilage and well differentiated bone. x155.



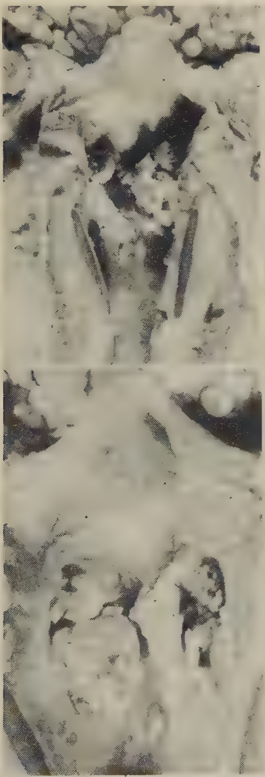
Proliferative chondritis. A smooth hard mass occluding three fourths of the subglottic and upper tracheal lumen in a 23 year old woman. Thirteen months' history following acute infection. Proliferating fibroblasts, giant cells, ragged fibrocartilage. x150.



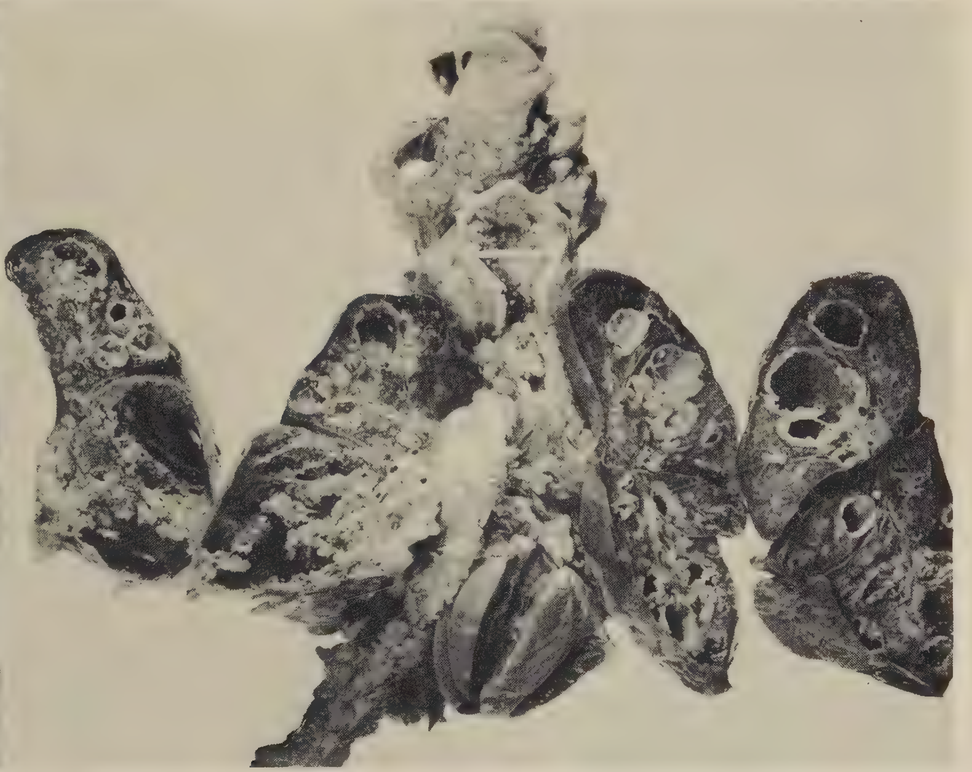
Solitary papilloma in a site of predilection, anterior portion of vocal cord near anterior commissure. Firm polypoid tumor. Adult with hoarseness.



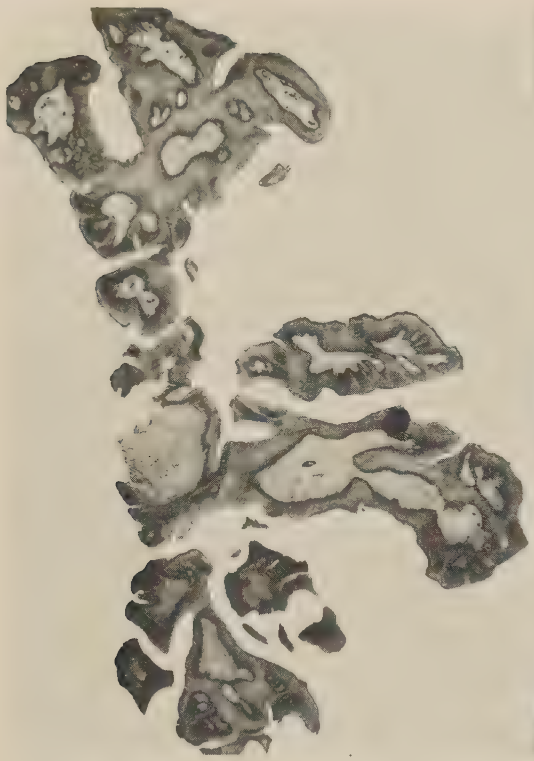
Multiple papilloma of cords, ventricles, ventricular bands and epiglottis. Five year old girl with attacks of aphonia and dyspnea. Died suddenly during night of asphyxia.



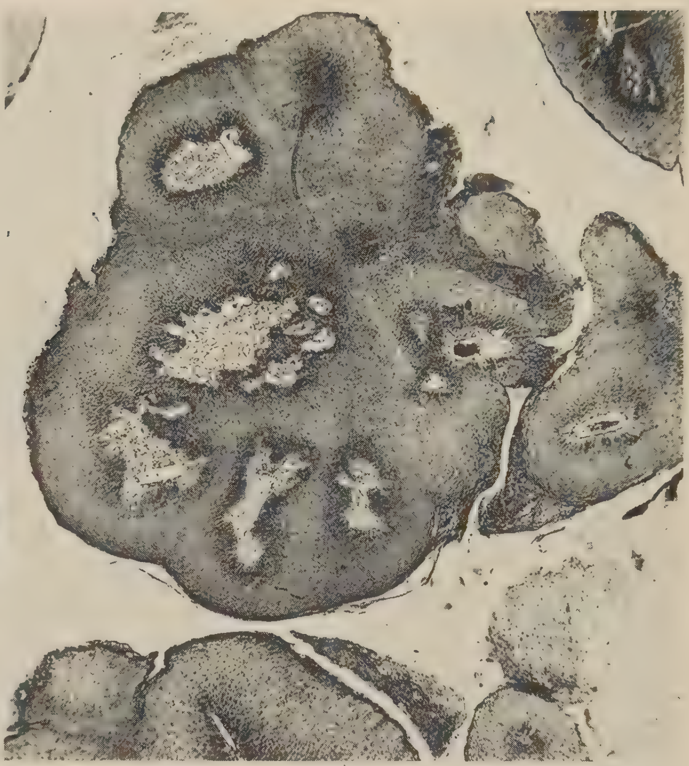
Multiple papilloma, congenital, of cords with subglottic extension and tracheal implants. Asphyxial death.



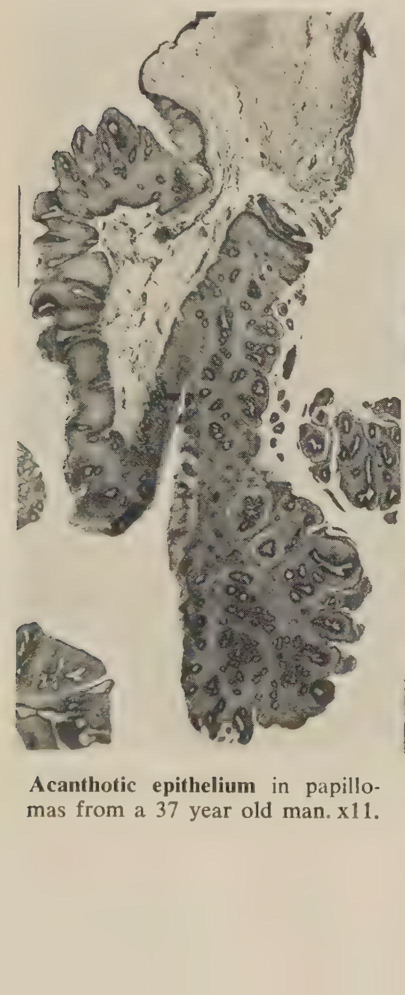
Diffuse papillomatosis of larynx and entire tracheobronchial tree with extension to pharynx, almost complete obstruction of trachea in an eight year old Negro. Cystic lung lesions lined by similar papillomatous tissue. Onset at four and one-half years with hoarseness progressing to aphonia and dyspnea. Tracheotomy tube required despite monthly removals of papillomas from larynx and pharynx. Chest roentgenogram revealed multiple cystic areas in both lungs. (J. Kirchner, New Haven, Conn. In Liebow's Fascicle No. 17, A.F.I.P. Atlas of Tumor Pathology.)



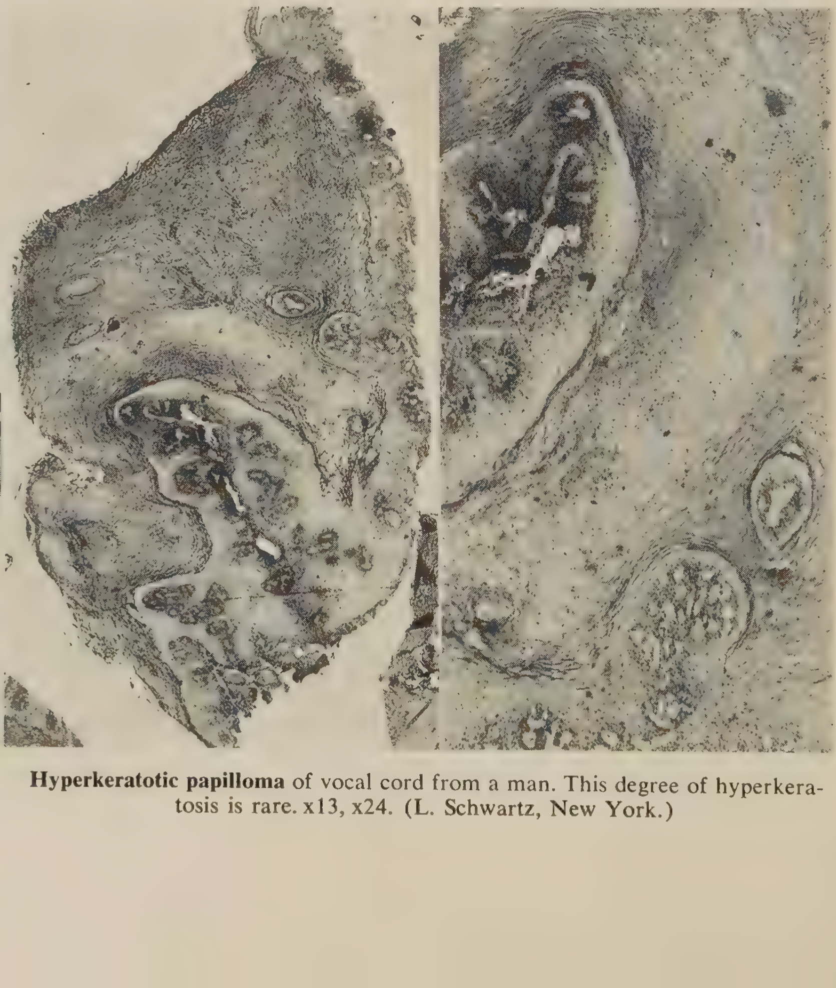
Typical histologic structure. Vascular connective tissue stalks covered usually by stratified squamous epithelium; occasionally by modified respiratory epithelium. x5. From 2 year old girl.



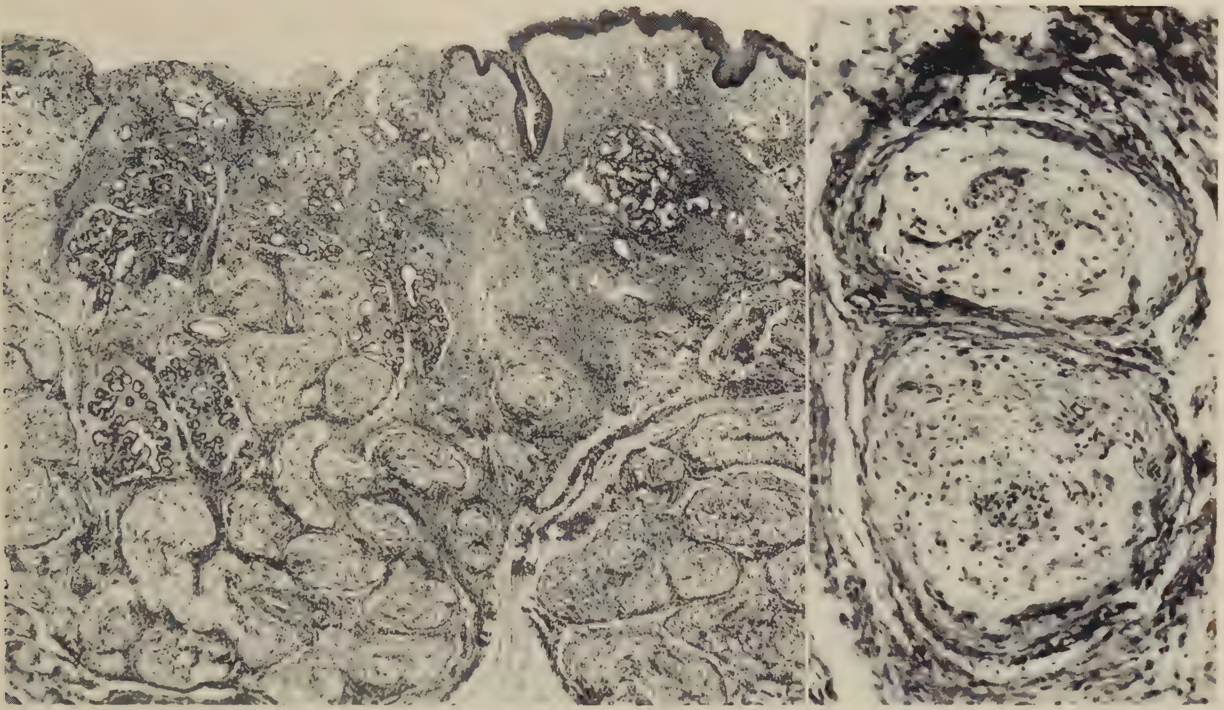
Active epithelial proliferation and hyperplasia in one of numerous recurrent papillomas removed in a two year period from an 8 year old boy. Other fragments showed moderate keratosis and some dyskeratosis. x48.



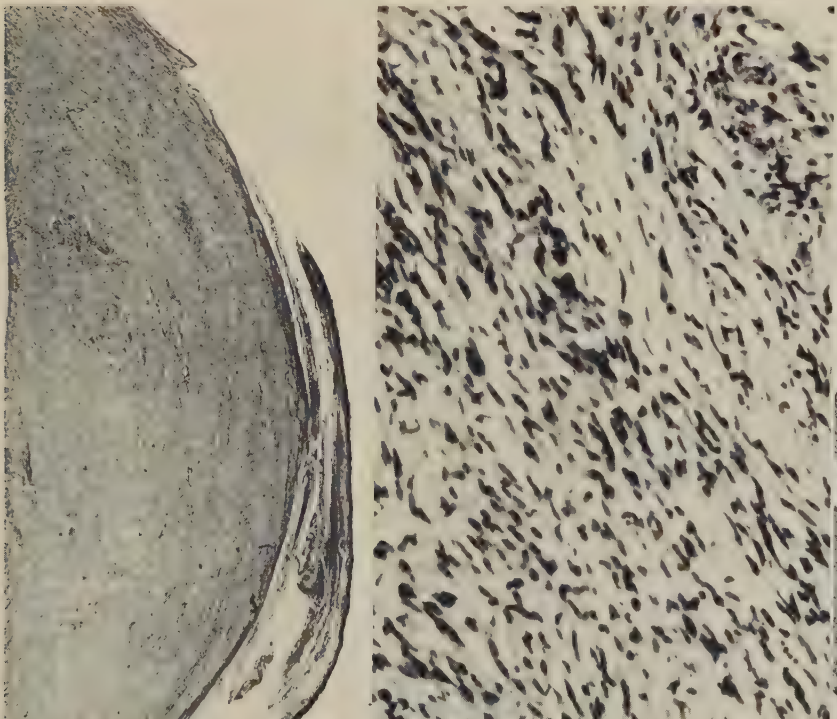
Acanthotic epithelium in papillomas from a 37 year old man. x11.



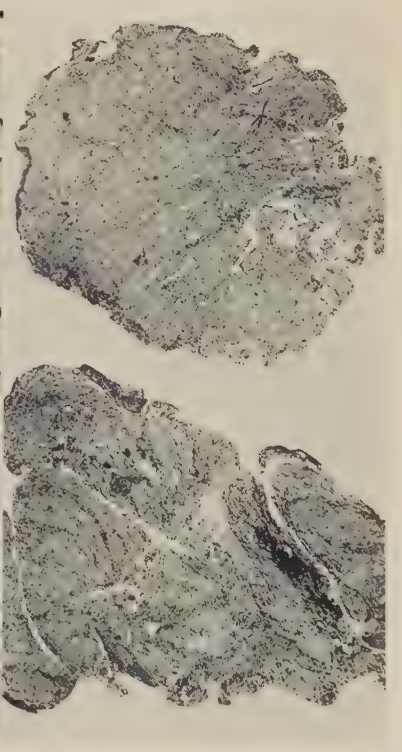
Hyperkeratotic papilloma of vocal cord from a man. This degree of hyperkeratosis is rare. x13, x24. (L. Schwartz, New York.)



Plexiform neuroma composed of irregular, enlarged fascicles of tangled nerve fibers. Mass with broad base attached to left arytenoid and seriously encroaching on airway of a 6 year old boy with no other lesions. History of respiratory difficulties for several years. x24. *Right:* poorly preserved nerve fibers in edematous nerve bundles with thickened sheaths. Unusual tumor. x24, x125. (L.H. Clerf, Philadelphia, Pa.)



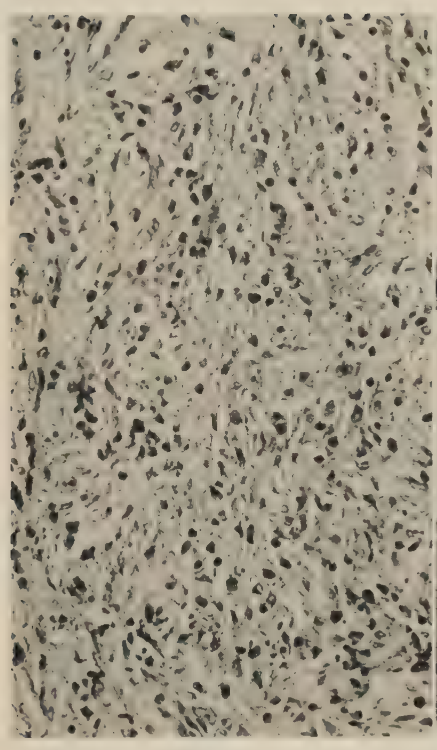
Fibroma of the epiglottis. *Left:* large, well encapsulated, solid tumor with smooth surface. Atrophy of overlying mucosa. x7. *Center:* well differentiated fibroblasts of uniform size and abundant collagen, hyalinized in some areas. x200. (H.P. Mosher, Boston, Mass.)



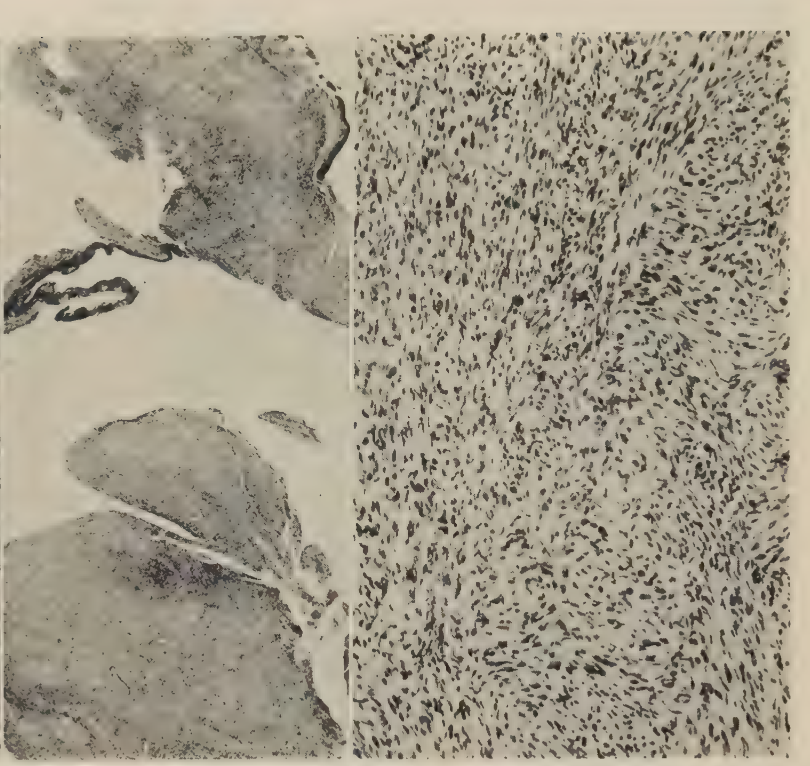
Inflammatory pseudotumor, first diagnosed fibroma. Sessile nodule below right cord in man, hoarse for 8 months. x10. (Detail, next plate.)

FIBROSARCOMA, LARYNX

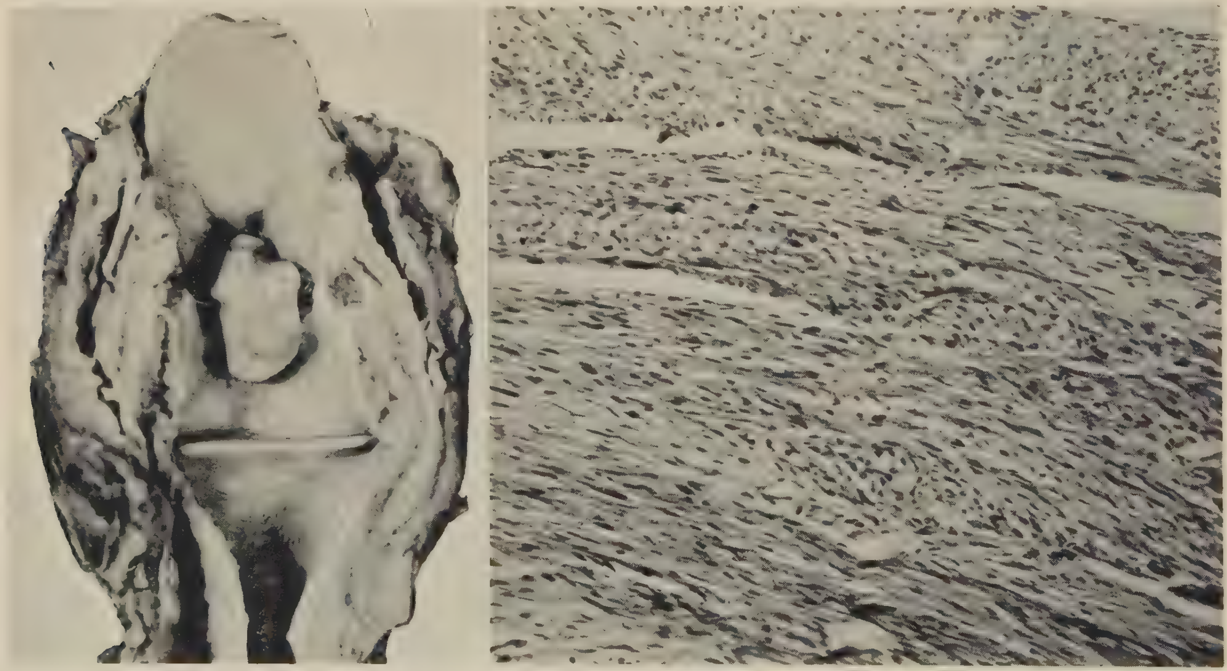
(WELL DIFFERENTIATED)



Inflammatory fibrous pseudotumor. Field from last case, previous plate. Reparative fibroblastic proliferation; diffusely scattered plasma cells, histiocytes, and lymphocytes. x275.



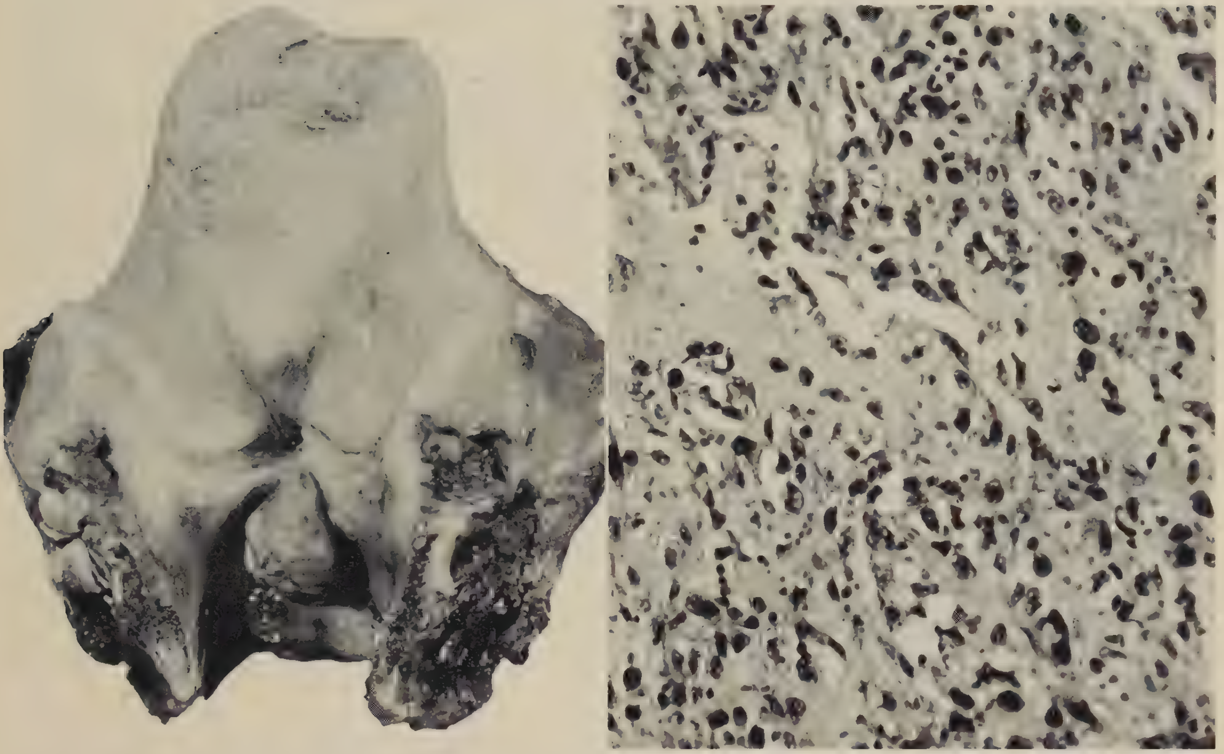
Fibrosarcoma of low grade malignancy. *Left:* two biopsy fragments of firm cellular, polypoid mass from anterior subglottic area in 44 year old woman with increasing hoarseness. x13. *Right:* bundles of delicate spindle-shaped fibroblasts and connective tissue fibers; very rare mitotic figure. x75.



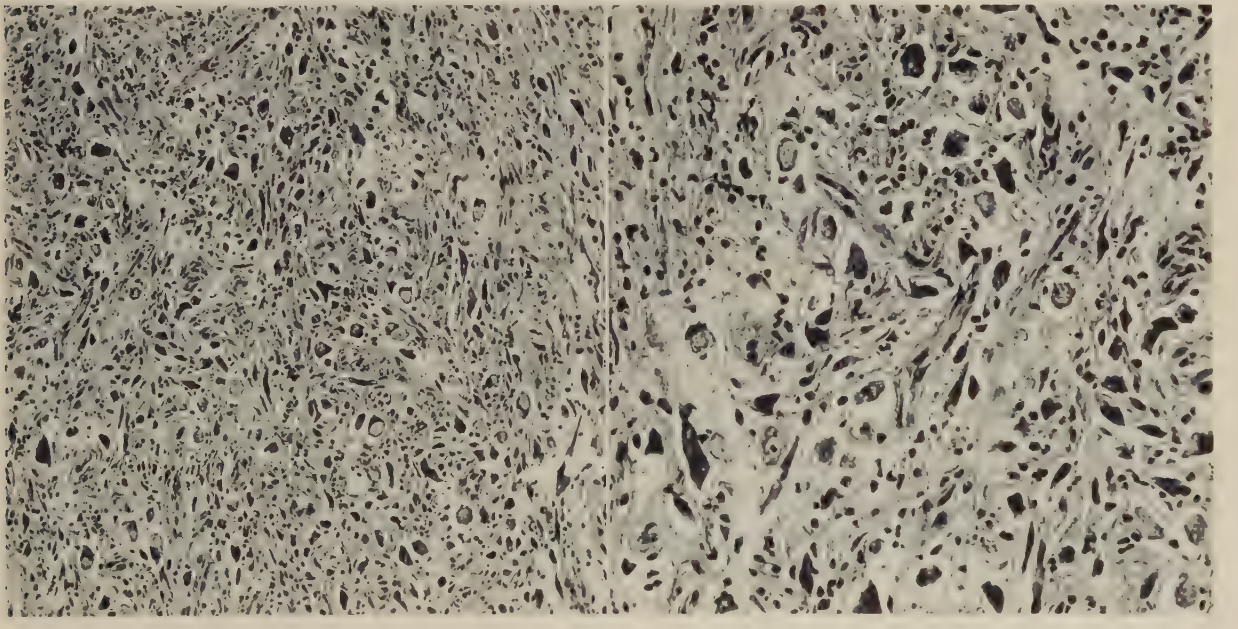
Fibrosarcoma, well differentiated. Large pedunculated tumor attached to anterior commissure, caused acute asphyxial death of a 50 year old man, hoarse for several months. No metastasis. Interlacing bundles of prominent connective tissue fibers; uniform fusiform cells; only occasional mitosis; thin-walled vascular spaces. x100. Such well differentiated slowly growing fibrosarcomas do not metastasize. (C.W. Maynard and J.W. White, Pueblo, Colo.)

FIBROSARCOMA, LARYNX

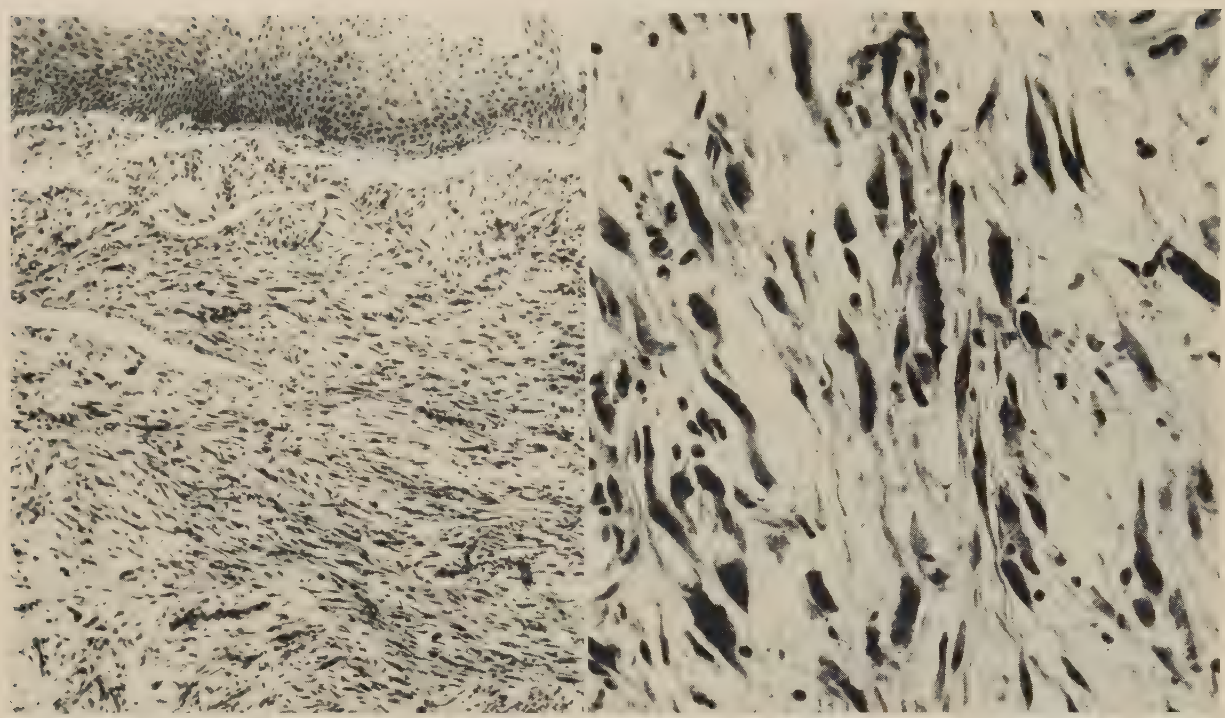
RHABDOMYOSARCOMA, HYPOPHARYNX



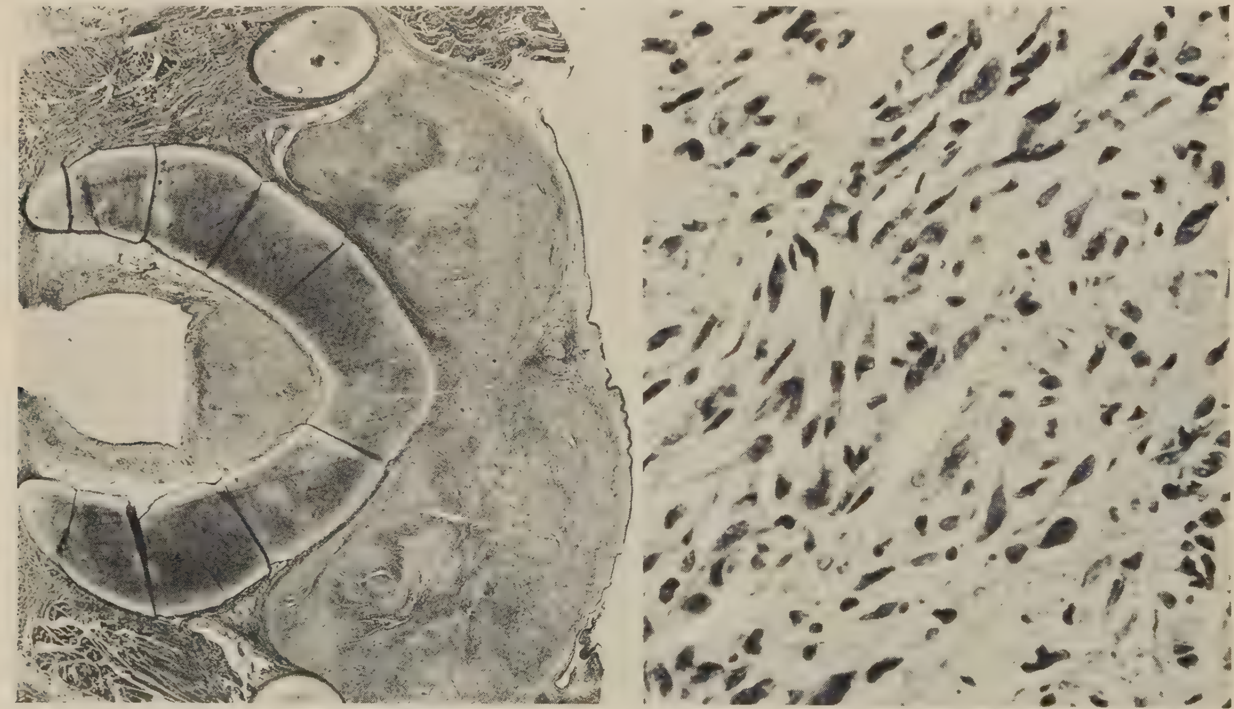
Fibrosarcoma, poorly differentiated, in a 72 year old man with attacks of hoarseness. *Left:* pedunculated polypoid mass attached by narrow base to anterior commissure. Extensive squamous metaplasia and hyperplasia of all laryngeal mucosa. *Right:* much of tumor was well differentiated; but many areas like this field, contained more plump, pleomorphic cells with hyperchromatic nuclei and very frequent mitoses. x275. Died four years after laryngectomy of undifferentiated carcinoma of lung not related to laryngeal lesions. (W.D. Dolan, Arlington, Va.)



Rhabdomyosarcoma. Large polypoid mass in left hypopharynx of a 50 year old woman extensively invaded the pharyngeal wall. Pleomorphic structure with rounded, ribbony, and strap-shaped cells, and numerous bizarre giant and multinucleated forms. Eosinophilic cytoplasm and processes frequently granular and fibrillar. No distinct cross striations (a rare finding in rhabdomyosarcomas of adults). x115, x235. (J.A. Murtagh and R.K. House, Hanover, N.H.)



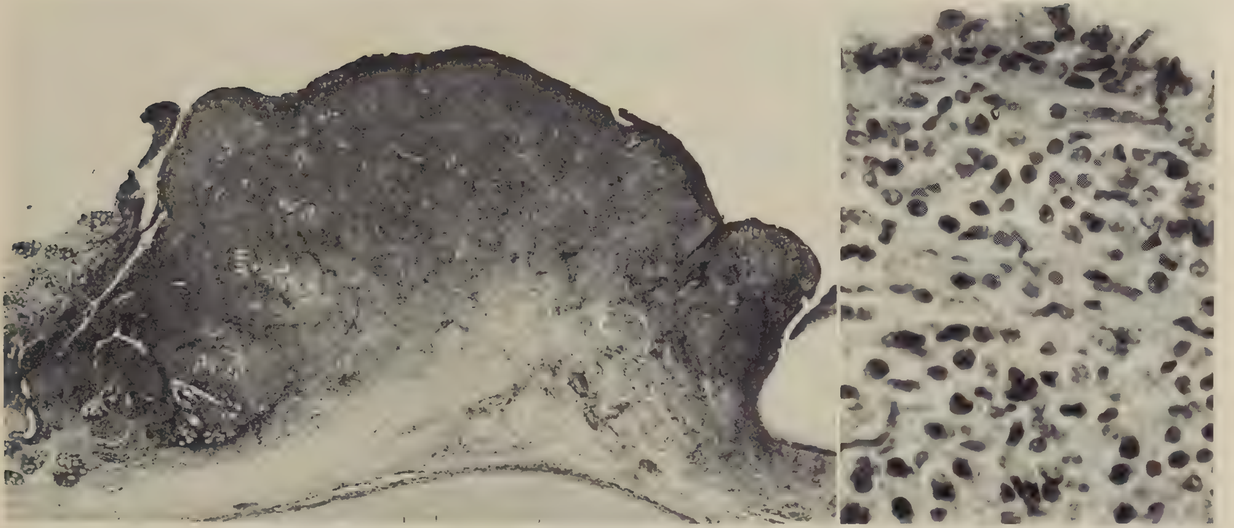
Rhabdomyosarcoma in 10 year old boy with hoarseness for several months; progressive dyspnea and dysphagia for several weeks. Firm mass, partially occluding glottis and arising from true cord, was completely resected by laryngofissure; had not recurred four years later. Cells predominantly long ribbony and strap-shaped forms, with frequent bizarre hyperchromatic nuclei. x115, x400. (H.N. Glick, St. Louis, Ann. Otol., Rhin. & Laryng. 53: 669, 1944.)



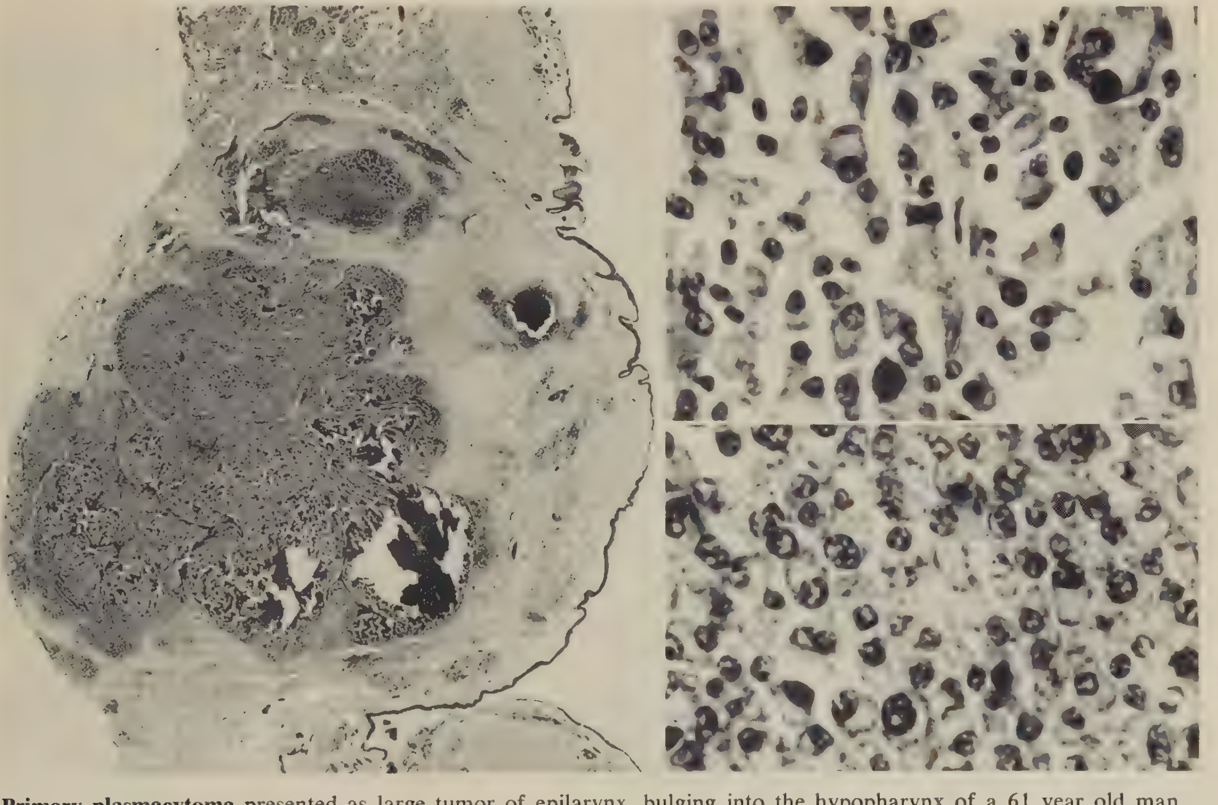
Embryonal rhabdomyosarcoma, congenital, in infant who lived one and one-half days. *Left:* section through cricoid cartilage, inferior horns of thyroid cartilage (top and bottom), and main portion of mass. It replaced posterior cricoarytenoid muscles, filling the posterior hypopharynx and constricting the proximal esophagus; extended around cartilages to the posterior intralaryngeal wall; invaded nerves and adjacent muscle. *Right:* partly differentiated field containing cells with large irregular, hyperchromatic nuclei and brightly eosinophilic processes or granular cytoplasm, as well as small oval and spindle cells. x435.

RETICULUM CELL SARCOMA

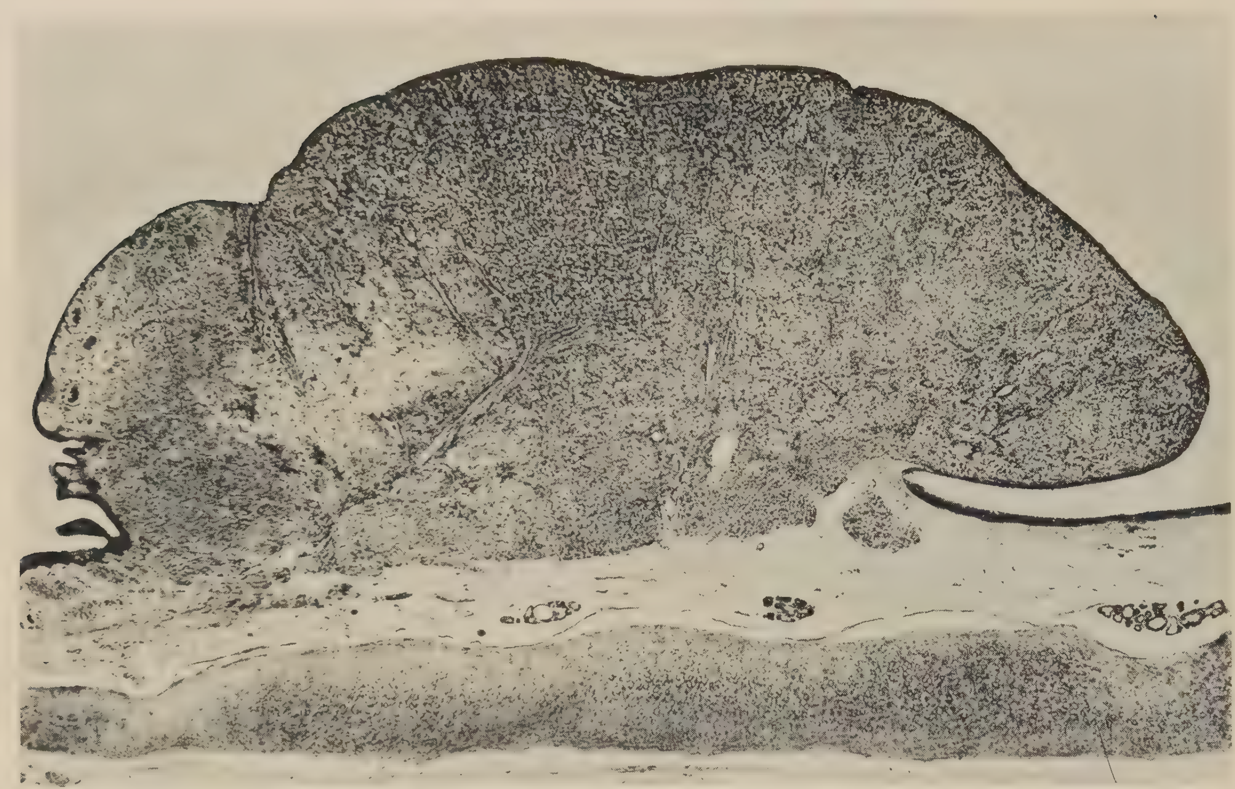
EXTRAMEDULLARY PLASMACYTOMA



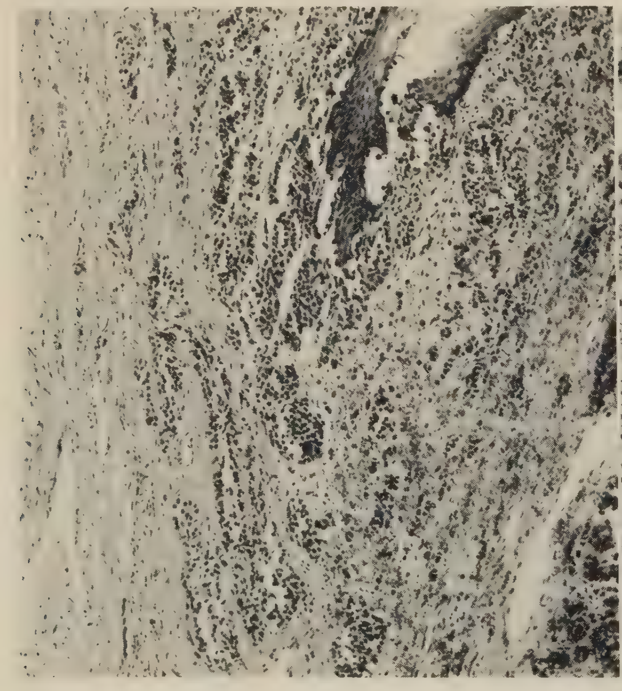
Reticulum cell sarcoma extensively infiltrated subglottic, ventricular and true cord and ventricular mucosa of 17 year old boy. Four months after "loss of voice," focal ulceration led to fatal hemorrhage. *Left:* thyroid cartilage at bottom, part of cricoid at right. Note partially preserved and atrophic glandular structures (left) and muscle bundles (right), widely separated by the dense cellular infiltrations. x8. *Right:* surface of tumor. Discrete cells with prominent nucleoli; numerous mitoses. x475. Silver stains demonstrated argyrophil fibrillar network considered "typical" of this form of malignant lymphoma. (R.H. King and B.J. McCloskey, Jacksonville, Fla.)



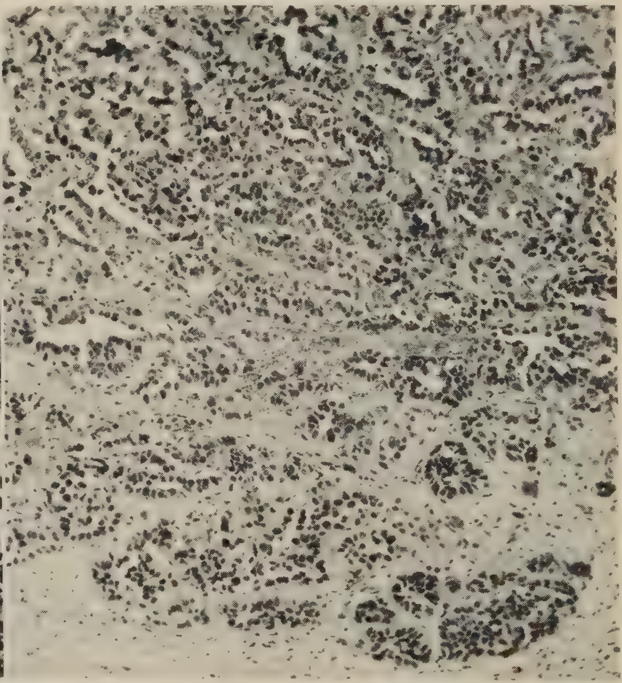
Primary plasmacytoma presented as large tumor of epilarynx, bulging into the hypopharynx of a 61 year old man, hoarse for six months. Surface epithelium at the right; resected margin at the left; normal mucosa at top and bottom. x7. *Right:* in this case, poorly differentiated obviously neoplastic cells resembling plasma cells. Marked variation in size, shape, cytoplasmic content; binucleate and trinucleate forms; atypical mitosis in center (*upper*, x540). Predominant cell type in the tumor, indistinguishable from that seen in many cases of plasma cell myeloma, in *lower* field. x600. (J.W. Leichliter, Cincinnati, Ohio)



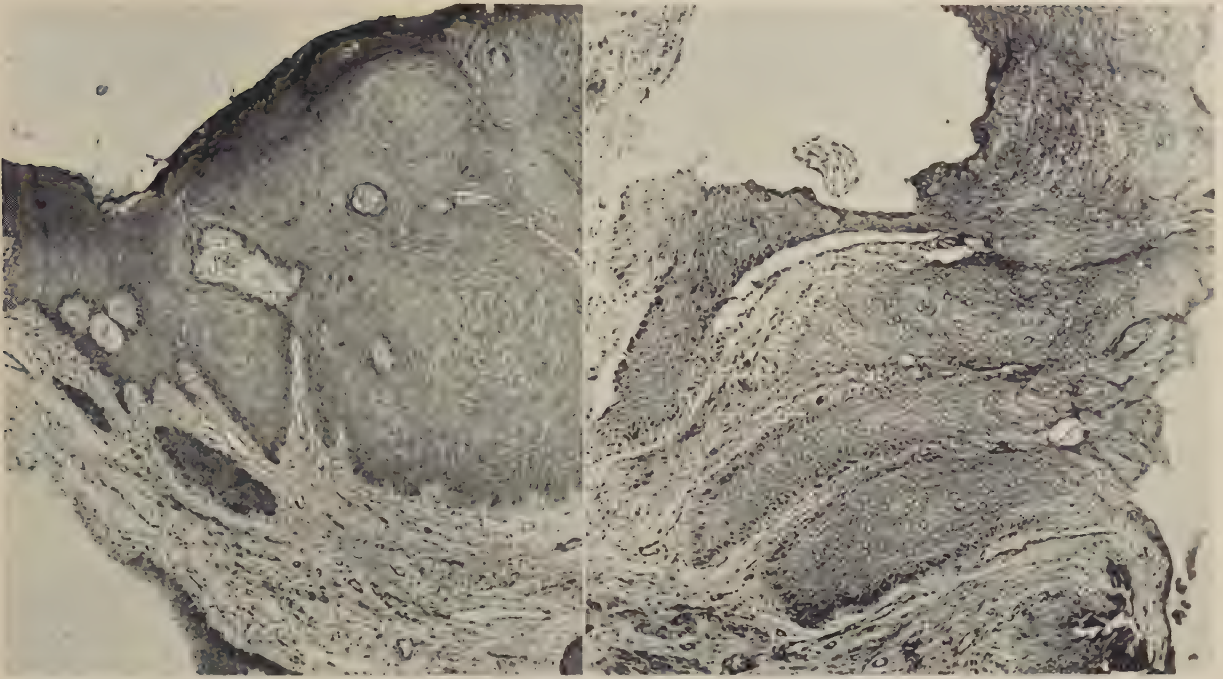
Tumor initially diagnosed adenoma or low grade adenocarcinoma. Reddish, mushroom-shaped growth, about 1x1x0.6 cm., on laryngeal surface of epiglottis, from a 37 year old man with hoarseness and slight cough for four months. Cellular tumor appears superficial; infiltration at base with lymphatic permeation more evident in other sections. Epiglottic cartilage at bottom. x14. Cervical metastases removed two years later by radical neck dissection.



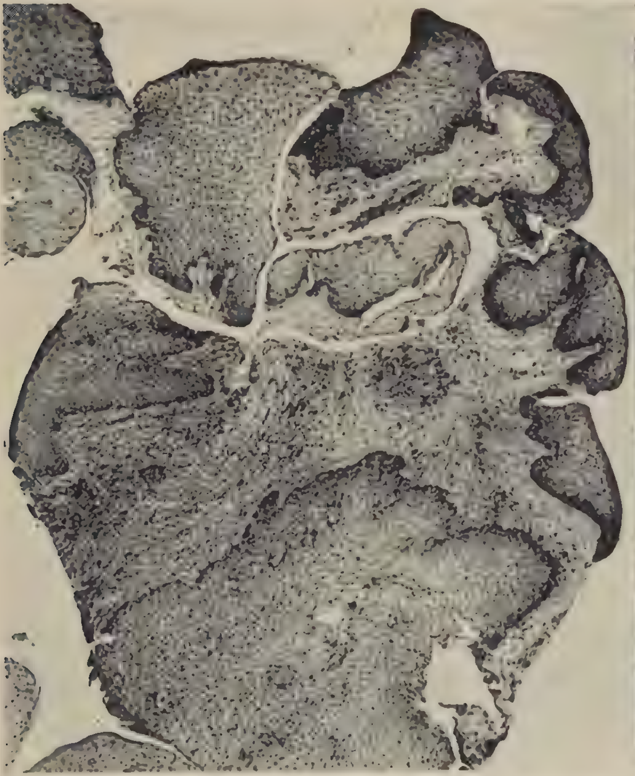
Lateral margin of tumor. Cords and strands of nevoid cells with hyperchromatic nuclei, suggestive of the true structural pattern of the neoplasm. No melanin pigment. Note "junctional change" at surface. x91.



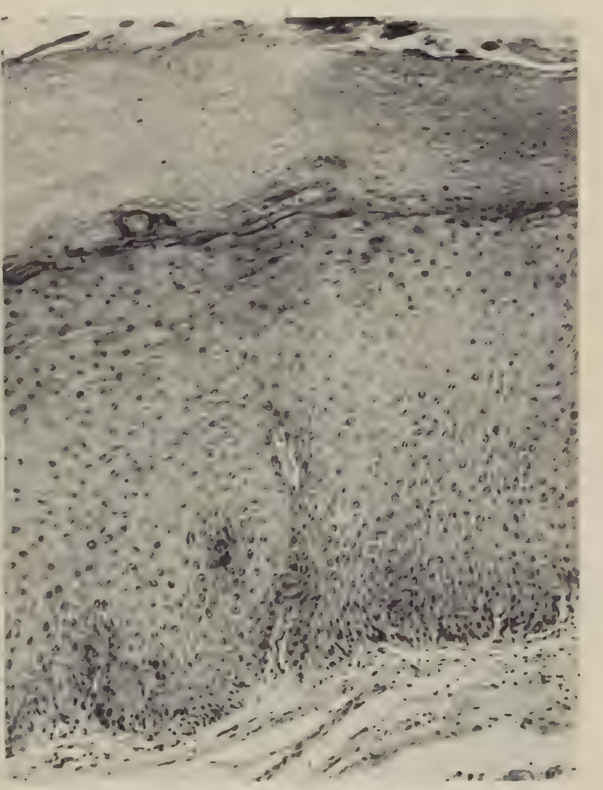
Pseudoglandular pattern, present in large areas of this nonpigmented tumor, occurs in some malignant melanomas. Frequent mitoses, cellular variation in size and shape, occasional large atypical cells in all fields. x125.



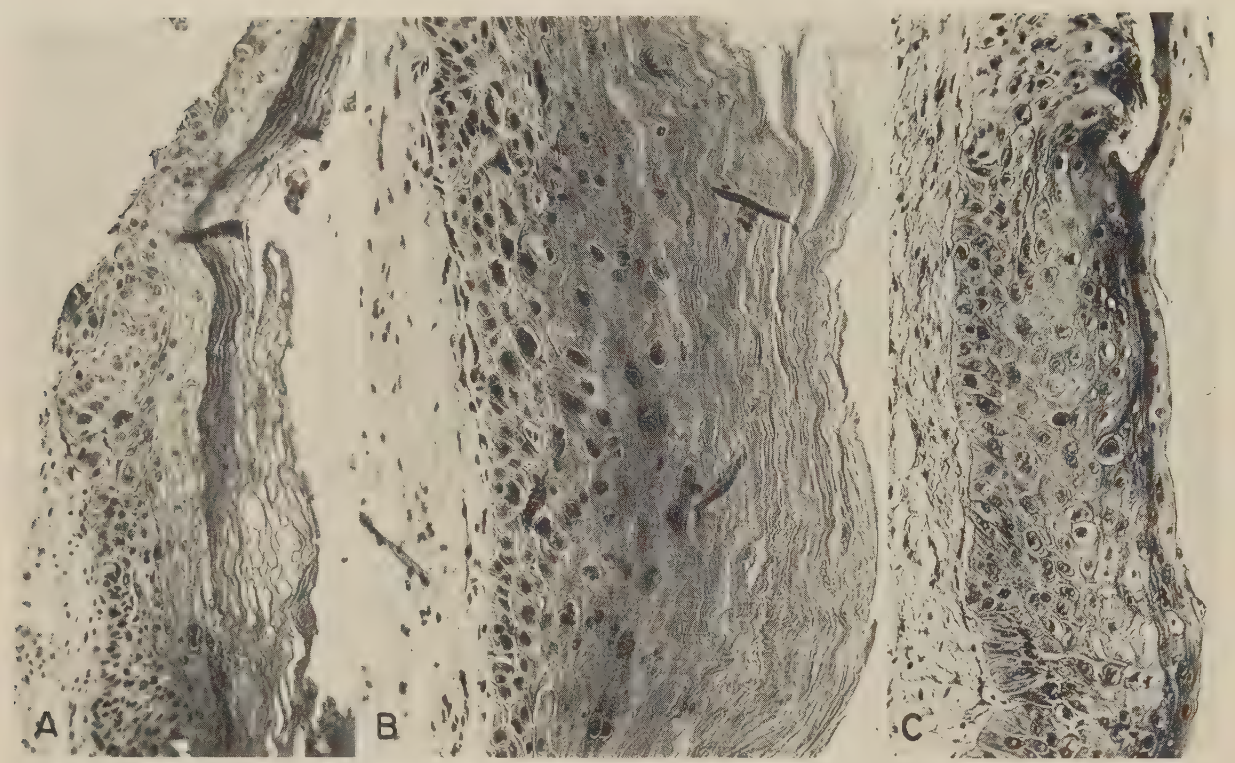
Epithelial hyperplasia, pronounced, and slight keratosis in biopsy fragments from a 61 year old man. Acanthosis, intact basal layer; no dyskeratosis; no mitoses. Not a papilloma, though so diagnosed. x55, x75. Subsequent biopsies from same patient in next plate.



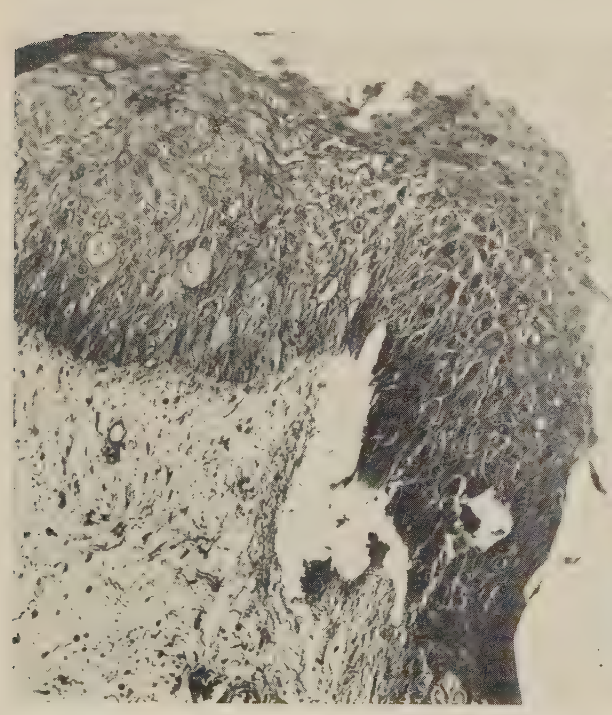
Focal epithelial hyperplasia and slight keratosis, but orderly maturation of epithelium. Dense chronic inflammatory stromal exudate. 2 mm. nodule on vocal cord from 34 year old man, hoarse for three months. x48.



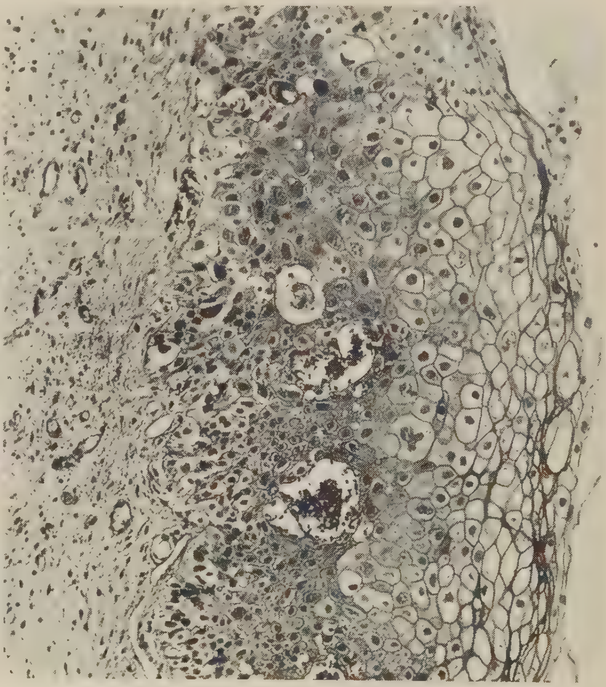
Marked acanthosis and keratosis; no dyskeratosis or mitoses. x75. Clinical diagnosis, leukoplakia. Anterior third of both cords thickened in 47 year old man with hoarseness. x75.



Leukoplakia, vocal cord. A, B, C. Well defined basement membrane; pronounced dyskeratosis with cells containing hyperchromatic nuclei, showing loss of polarity, fairly frequent mitoses; parakeratosis and hyperkeratosis. x145, x210, x185. **C.** is field from second biopsy of case that showed epithelial hyperplasia on preceeding plate.

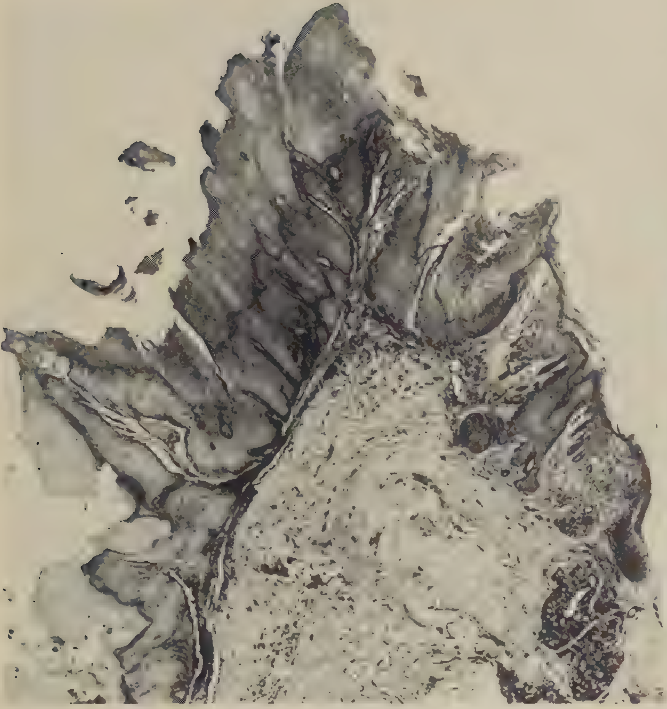


Leukoplakia with possible focus of intraepithelial carcinoma at right. Conspicuous abnormal mitoses; atypical giant and multinucleated cells in all layers to surface. Same biopsy specimen as **C.** x125.

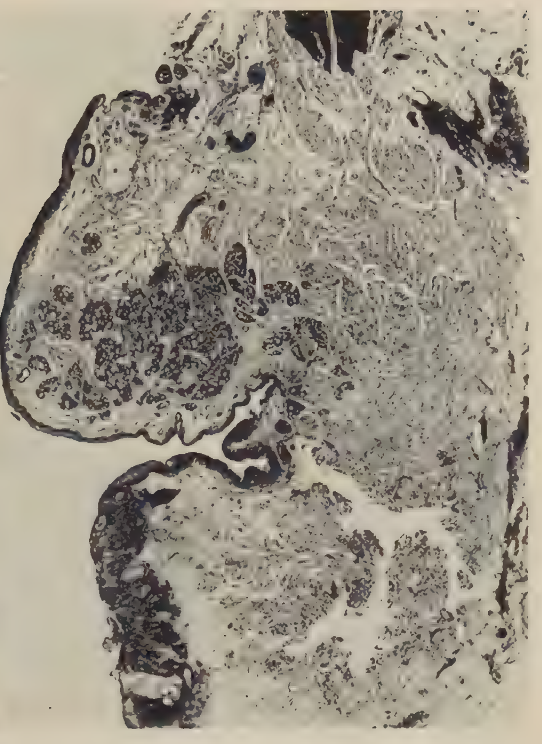


Intraepithelial carcinoma. Field adjacent to frank early invasive carcinoma in third biopsy of same case. Proliferation in basal layers, bizarre cells, frequent abnormal mitoses. Note tripolar nucleus. x190.

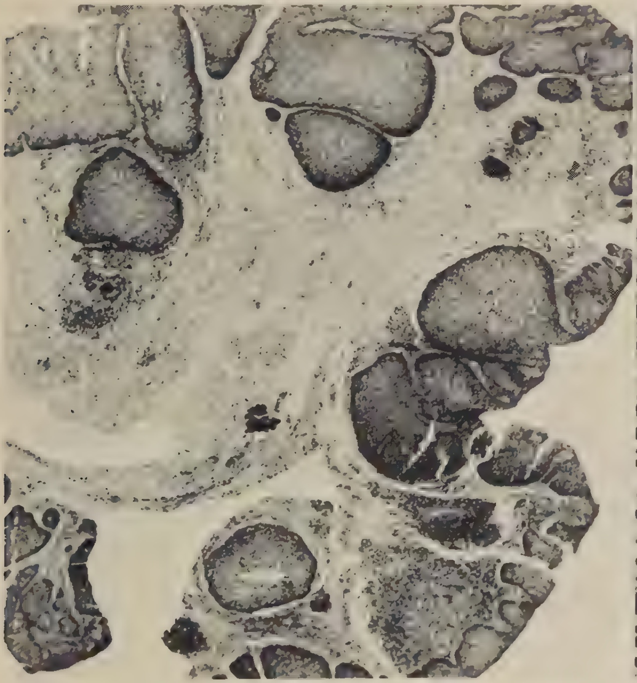
LEUKOPLAKIA–EARLY CARCINOMA



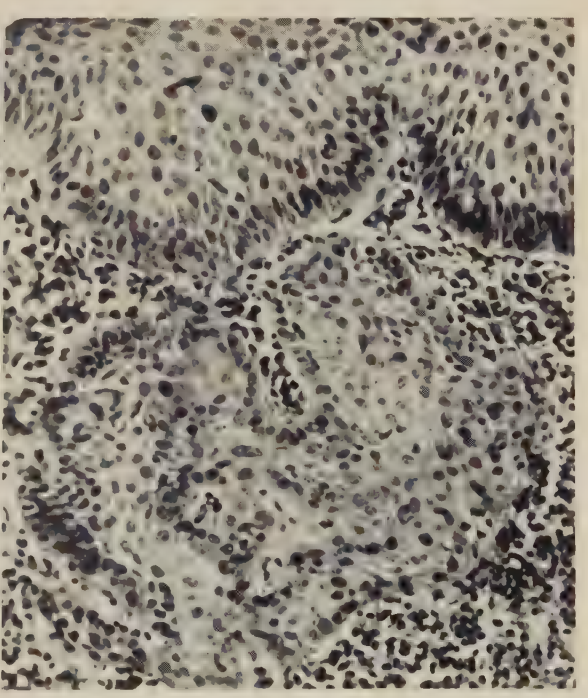
Verrucous leukoplakia, vocal cord. Wartlike acanthosis, parakeratosis and hyperkeratosis. Well defined basal cell layer. Dyskeratosis particularly pronounced on the right. (F. Lederer.)



Early carcinoma of true cord (lower left), with probable origin in leukoplakic epithelium. Leukoplakia of adjacent epithelium. Epithelium of false cord hyperplastic. (F. Lederer, Chicago, Ill.)

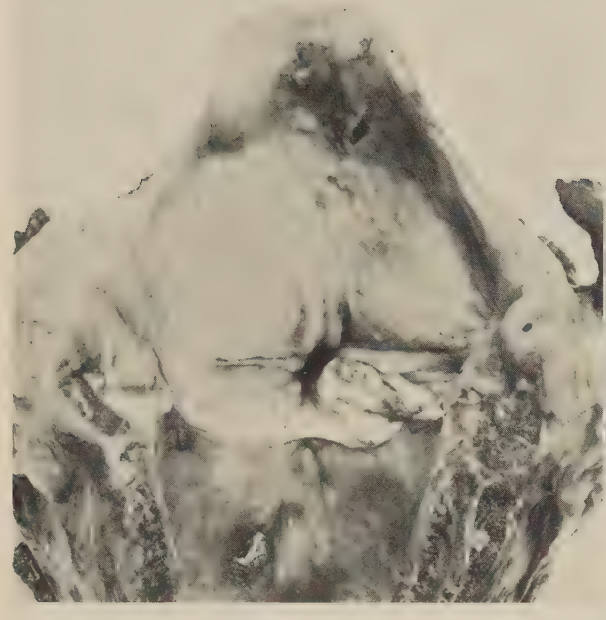


Papillomatous leukoplakia. No history of papillomatosis or laryngeal nodule, diagnoses suggested clinically because of polypoid configuration. Frequent mitoses and dyskeratosis. This histologic pattern may be seen in pachydermia laryngis. x40.

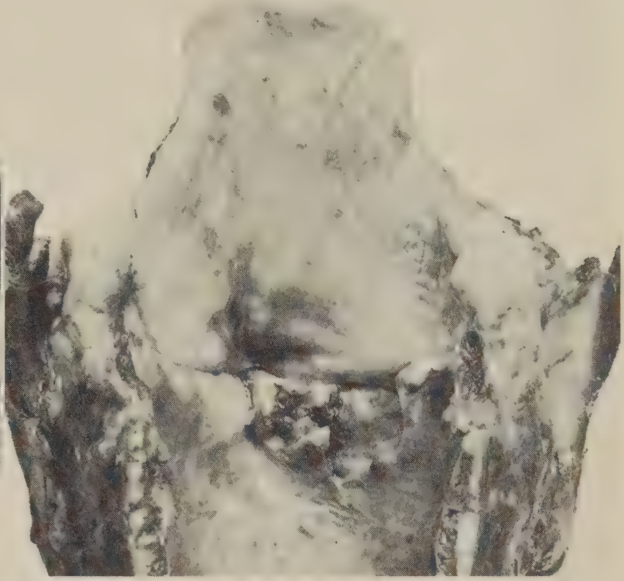


Very early carcinoma invading the stroma of same case. Magnified field of area indicated by arrow in *left* illustration. Infiltrating nests of cells with hyperchromatic nuclei and numerous mitoses. x205.

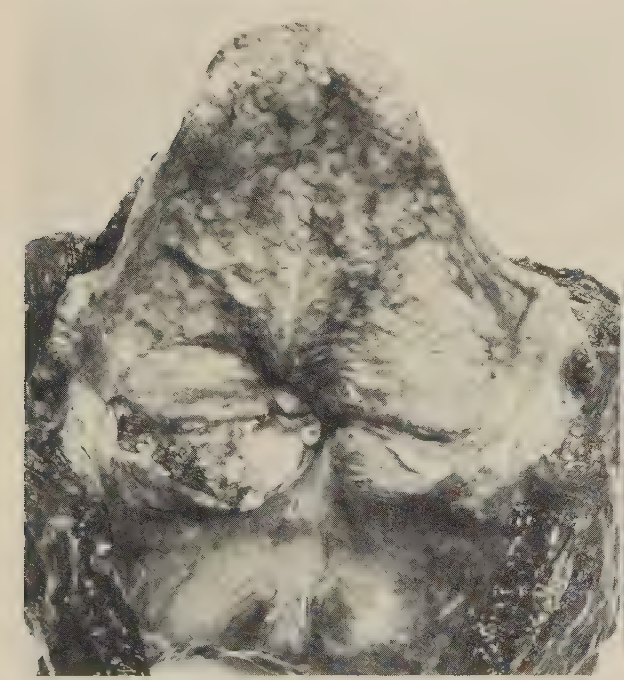
CORDAL CARINOMA; "INTRINSIC" CARCINOMA



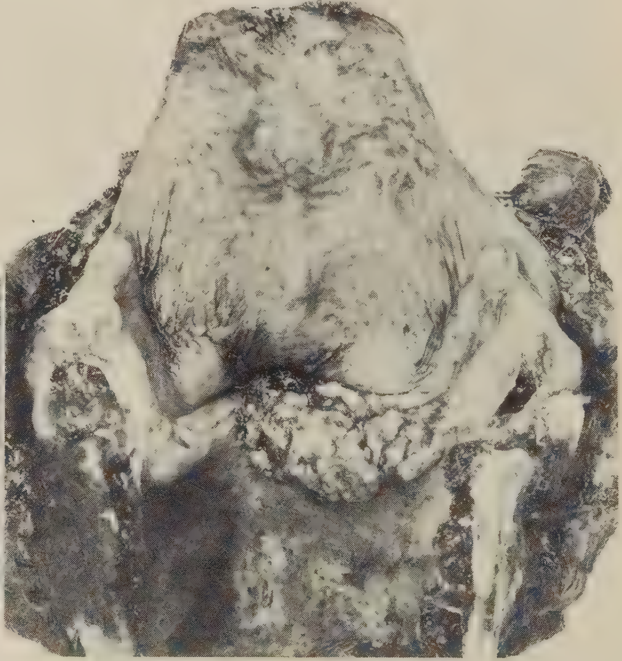
Pale nodular, nonulcerated mass of right vocal cord with subglottic extension across the anterior commissure to the subglottic area on the left side. From 52 year old man.



Extensively ulcerated, infiltrating tumor in a 57 year old man. Apparently arising in right vocal cord, it has extended to anterior commissure and is invading subglottic mucosa.



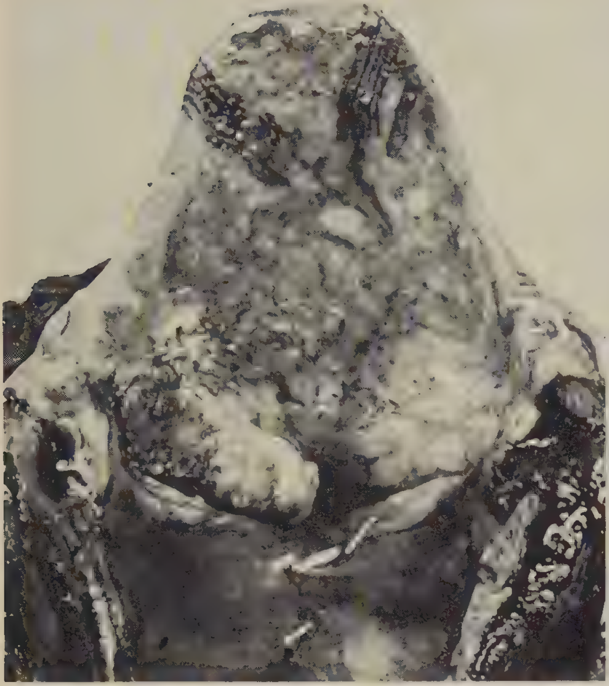
Bulky granular carcinoma, from a 59 year old man, involving entire left vocal cord to the anterior commissure. Part of the surface is necrotic, and there is neoplastic extension beneath intact mucosa at lower left.



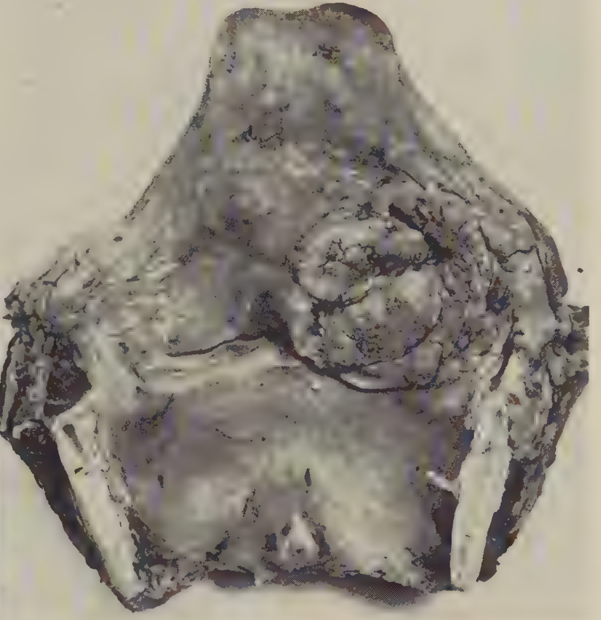
Fungating, cauliflower-like growth caused complete fixation of the right side of the larynx in a 59 year old man. It involves entire right true cord and anterior commissure to the anterior portion of the left cord.

These illustrations are *laryngectomy specimens* from male patients with presenting symptom of hoarseness, as is usual. All were epidermoid (squamous cell) carcinomas, as are approximately 96 per cent of laryngeal carcinomas in reported cases. (Courtesy of P. Holinger and E. Hirsch, Chicago, Ill.)

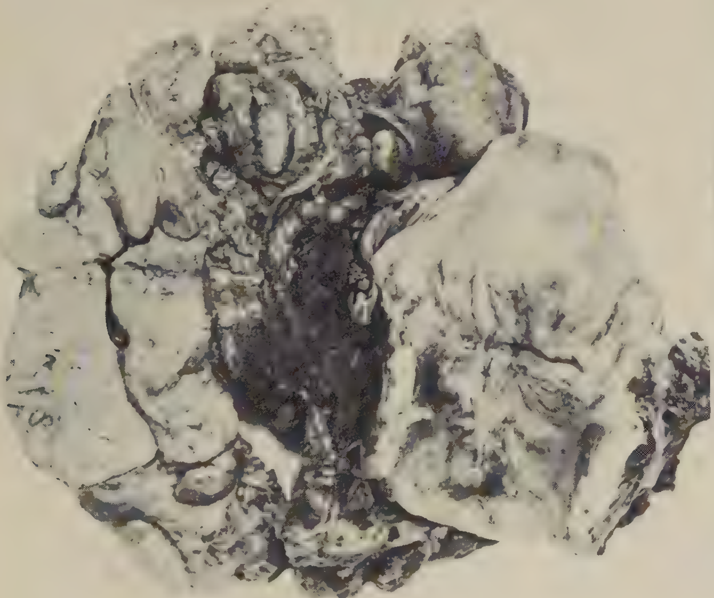
SUBGLOTTIC AND SUPRAGLOTTIC ("EXTRINSIC") CARCINOMA



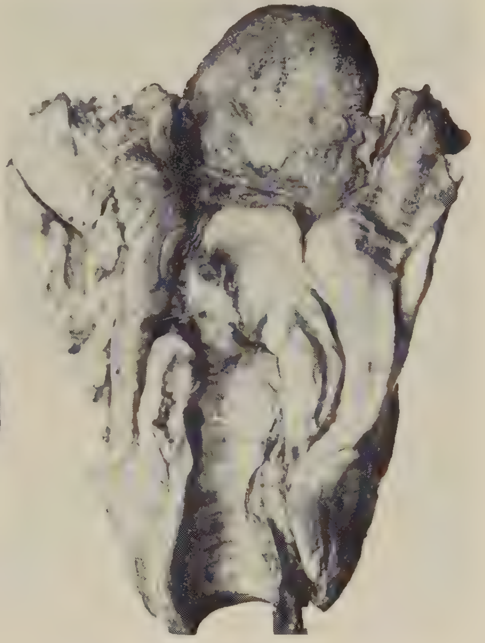
Supraglottic epidermoid carcinoma. Laryngectomy specimen from a 65 year old man. Origin in the left ventricular fold (false cord) is obvious, with extension medially to the anterior commissure. The true vocal cords are edematous, but uninvolved.



Supraglottic epidermoid carcinoma arising at base of epiglottis has extended laterally to the right aryepiglottic fold, inferiorly to the true cord. Though extensive, no clinical symptoms in a 40 year old man until one month prior to laryngectomy. (Both from E. Hirsch and P. Holinger.)



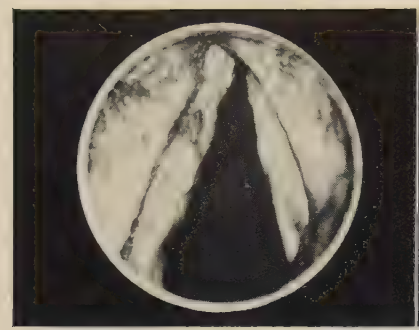
Massive cervical metastases from extensive subglottic neoplasm. Infiltrating epidermoid carcinoma has extended to left true and false cords in 65 year old woman. Laryngectomy specimen including part of first tracheal ring and left radical neck dissection. (E. Hirsch and P. Holinger, Chicago.)



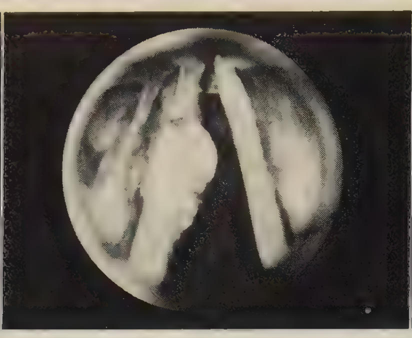
Extension to hypopharynx and metastasis to cervical lymph nodes. Primary epidermoid carcinoma of left true and false cords with supraglottic and subglottic extension. Autopsy specimen.

CARCINOMA, LARYNX

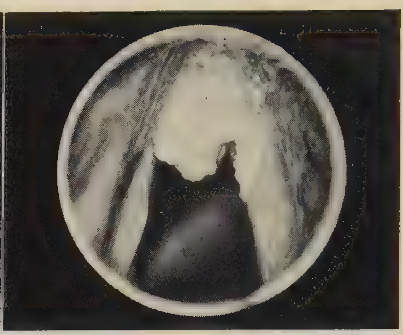
LARYNGOSCOPIC VIEWS–TRANSECTION



Small ulcerative carcinoma of anterior left vocal cord.

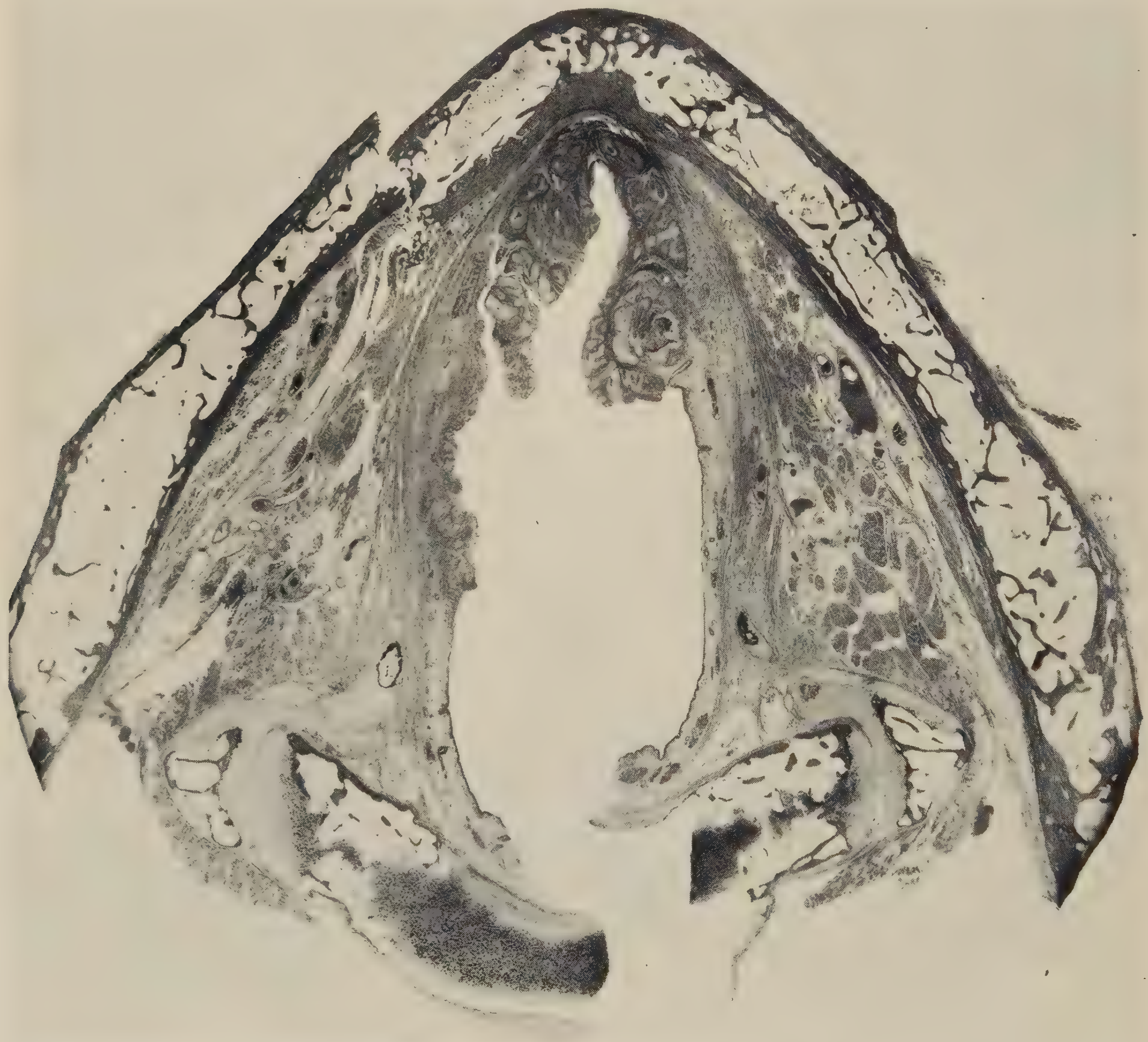


Early nodular carcinoma of middle third of left vocal fold.



Anterior commissure carcinoma involving both anterior vocal folds.

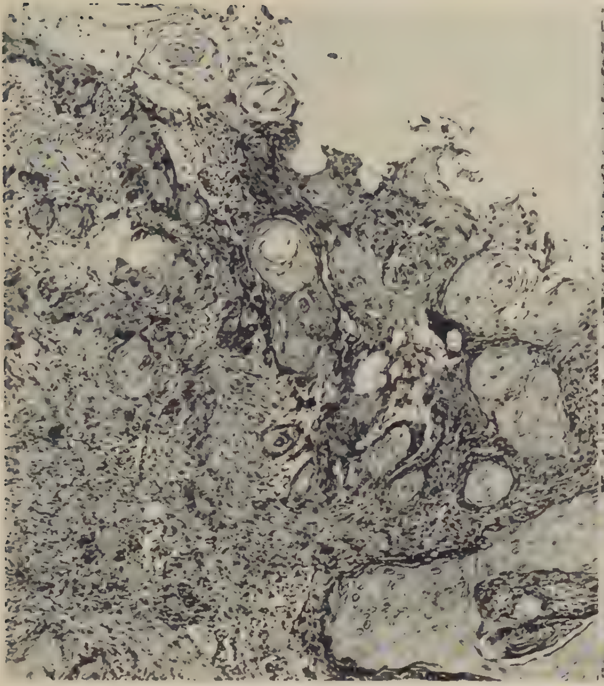
(Direct laryngoscopic photographs from P. Holinger.)



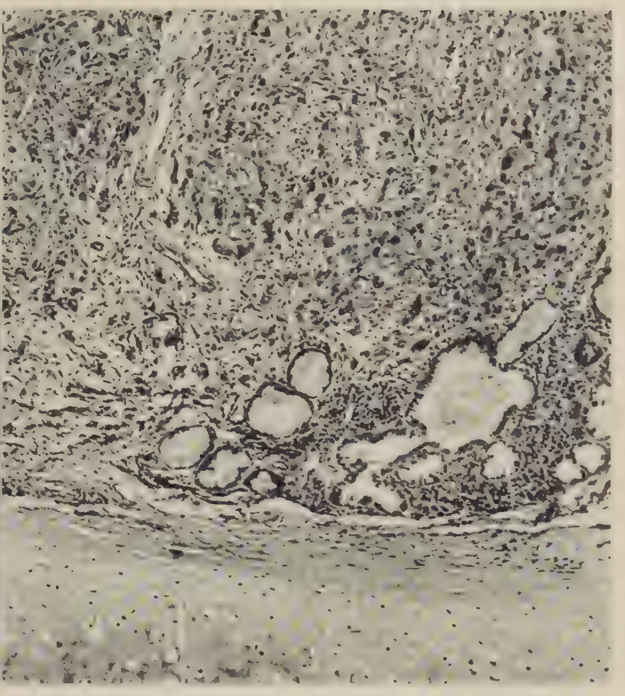
Epidermoid carcinoma, well differentiated, of the anterior commissure, anterior one third of the right true cord, and anterior two thirds of the left cord. Though covering a large surface, the neoplasm has not extensively invaded deeper structures and appears relatively superficial. Transection through laryngectomy specimen at level of vocal folds. x4½. (S.R. Guild and S.J. Crowe, Baltimore, Md.)

CARCINOMA, LARYNX

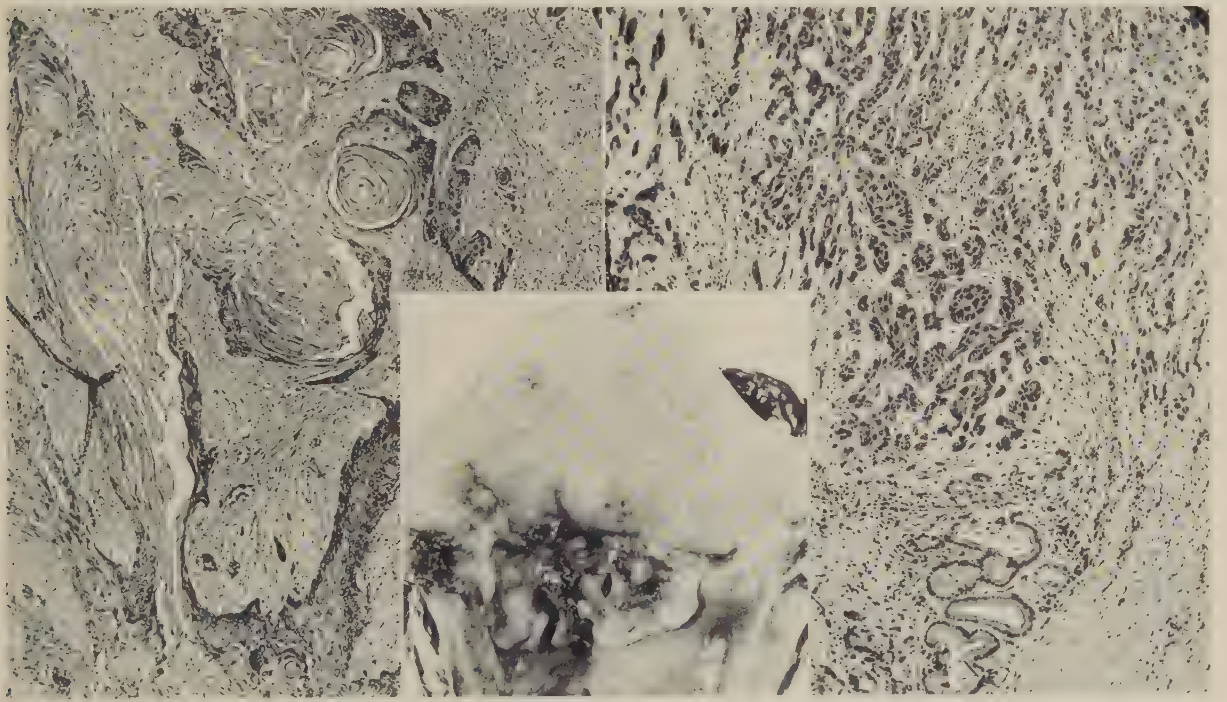
POSSIBLE FALLACY IN HISTOLOGIC GRADING



Well differentiated epidermoid carcinoma, with epithelial pearl formation, keratinization and rare mitoses, in laryngeal biopsy specimen taken after emergency tracheotomy. x70. Death with metastases to lymph nodes, heart, lungs, adrenals and liver.



Undifferentiated, diffusely infiltrating carcinoma in regional extension to trachea and thyroid and metasta from same patient. No keratinization; frequent atypical mitoses; hyperchromatic, often bizarre nuclei. Extension to trachea. x75.

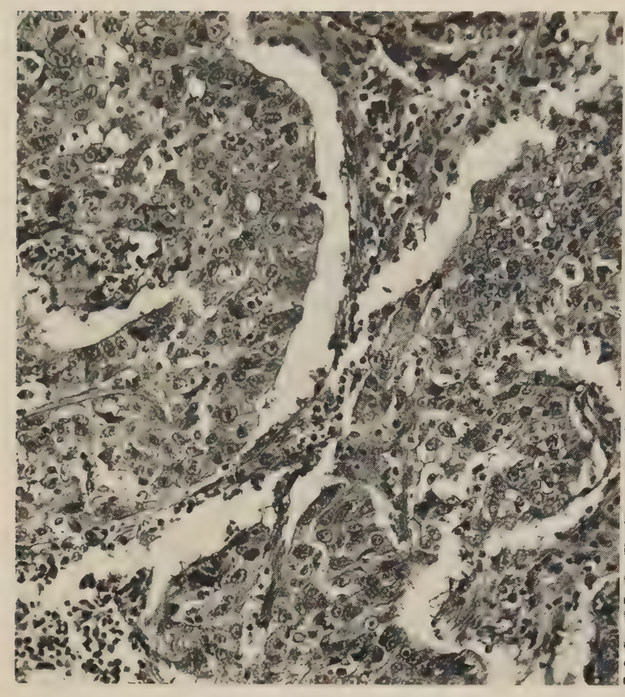


Inset: Laryngectomy specimen. Endolaryngeal carcinoma of true cords and anterior commissure with subglottic extension and obliteration of ventricle and invasion of left false cord above.

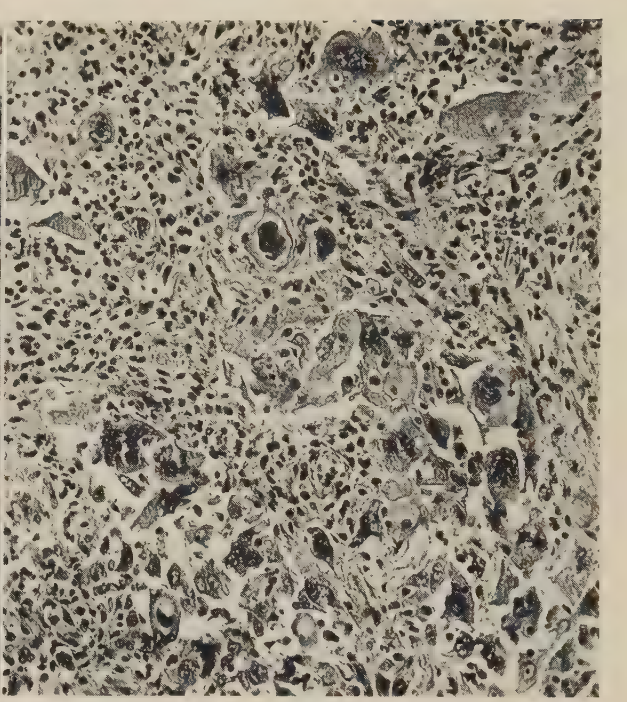
Well differentiated, keratinizing epidermoid carcinoma in superficial areas of a large section from the specimen. x62.

Poorly differentiated tumor in form of narrow strands and small nests invading stroma of deep portion of the same section. x75.

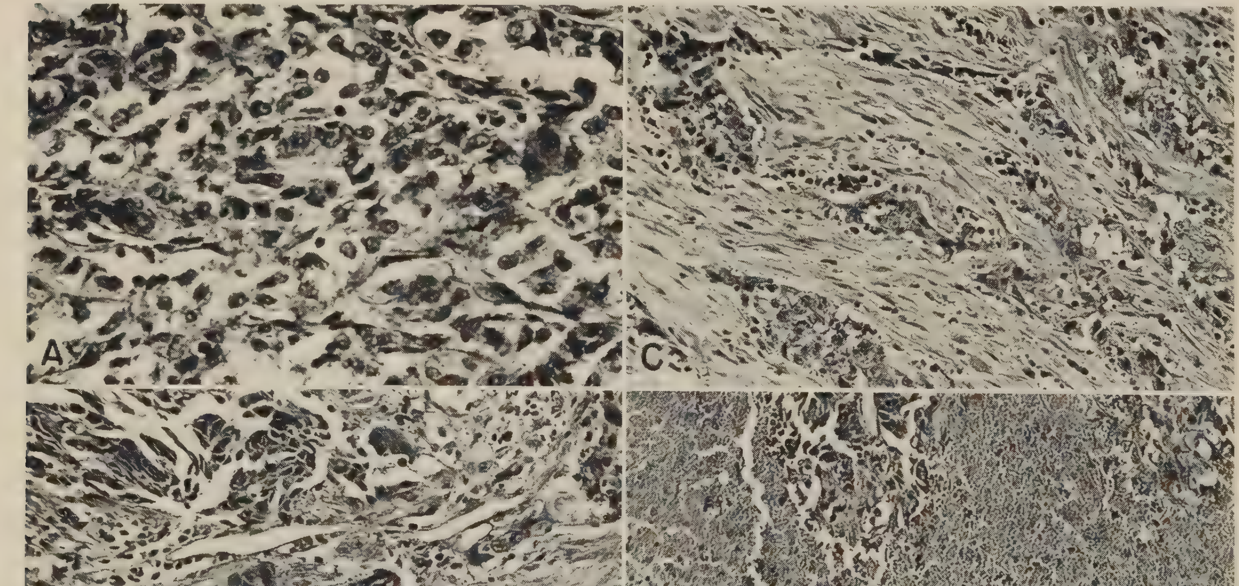
CYTOLOGIC AND STRUCTURAL VARIATION



Epidermoid carcinoma, poorly differentiated. The primary laryngeal tumor and massive cervical metastases showed striking variation in histologic structure. Moderately well differentiated focus above. x145.

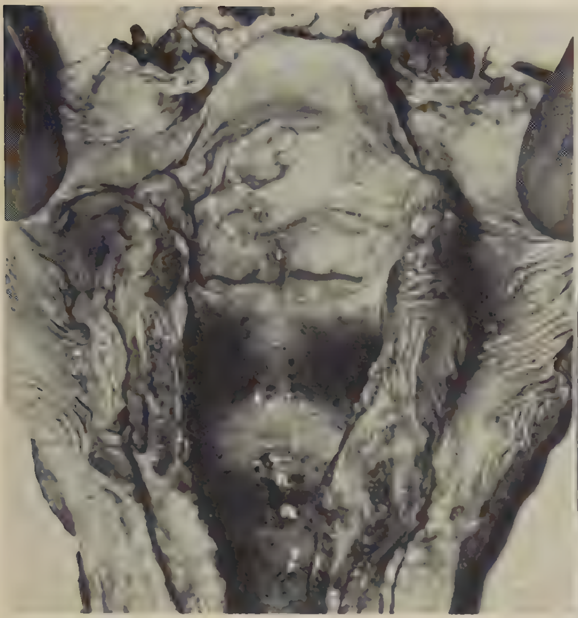


Pleomorphic pattern within carcinomatous extension to the thyroid gland. Bizarre dissociated cells; many giant and multinucleated cells; abnormal mitoses. Surrounding dense inflammatory exudate. x185.

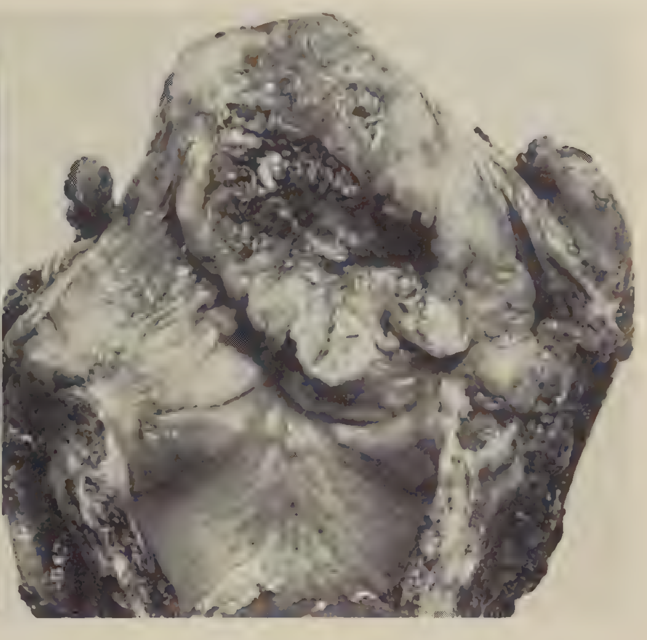


Variation in cell type and growth pattern. Same case illustrated above. **A.** Solidly cellular masses in pseudoalveolar pattern. Vesicular nuclei; abundant foamy or clear cytoplasm. x245. **B.** Cords and strands of irregular and spindle-shaped cells with hyperchromatic nuclei and little cytoplasm. x145. **C.** Area showing marked desmoplastic reaction. x125. **D.** Field from extensive area of necrosis. x90.

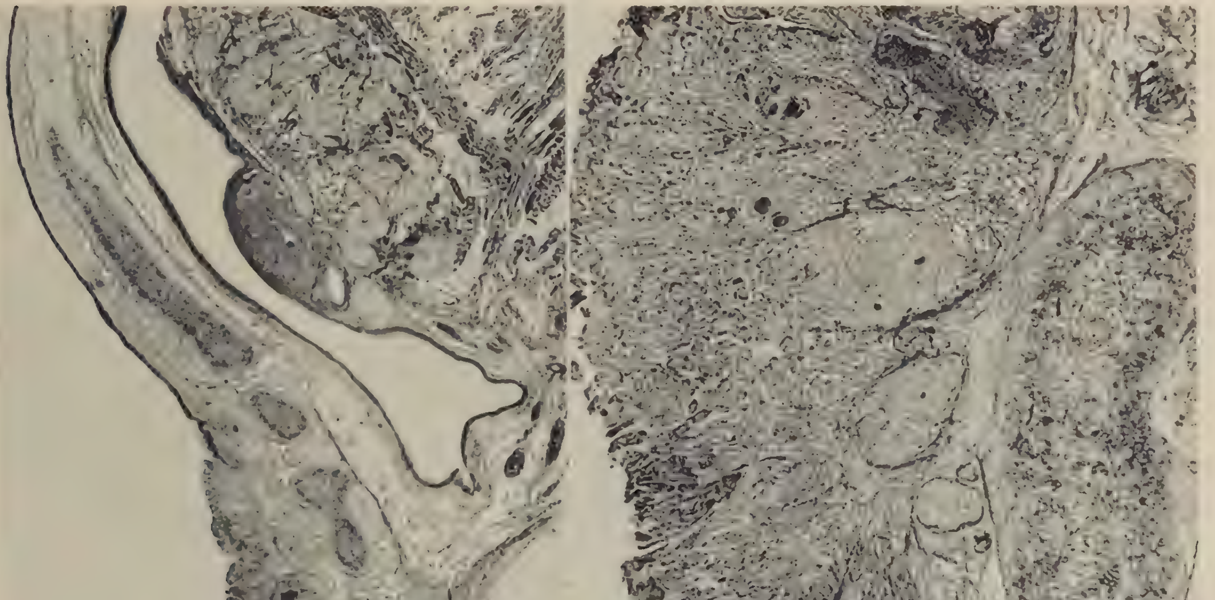
CARCINOMA, EPIGLOTTIS; SUPRAGLOTTIC CARCINOMA



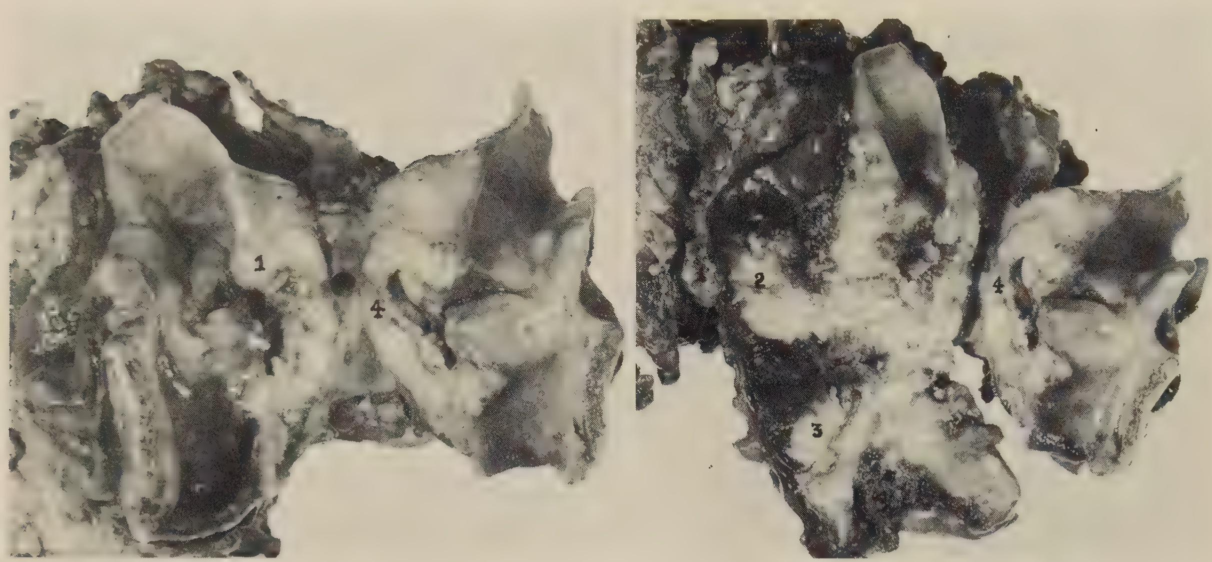
Primary carcinoma of the epiglottis. Incidental autopsy finding in 55 year old man who died of dissecting aortic aneurysm prior to cataract operation. Note petechial hemorrhages in subglottic mucosa. (Photography by Victor Landi, V.A.H., Wash., D.C.)



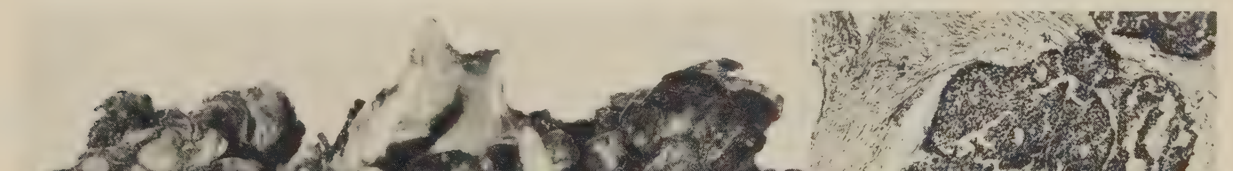
Extensive supraglottic carcinoma involves most of the laryngeal surface of the epiglottis, extending inferiorly to right false cord. The true cords are uninvolved. Symptoms for only brief period prior to laryngectomy. (E. Hirsch and P. Holinger, Chicago, Ill.)



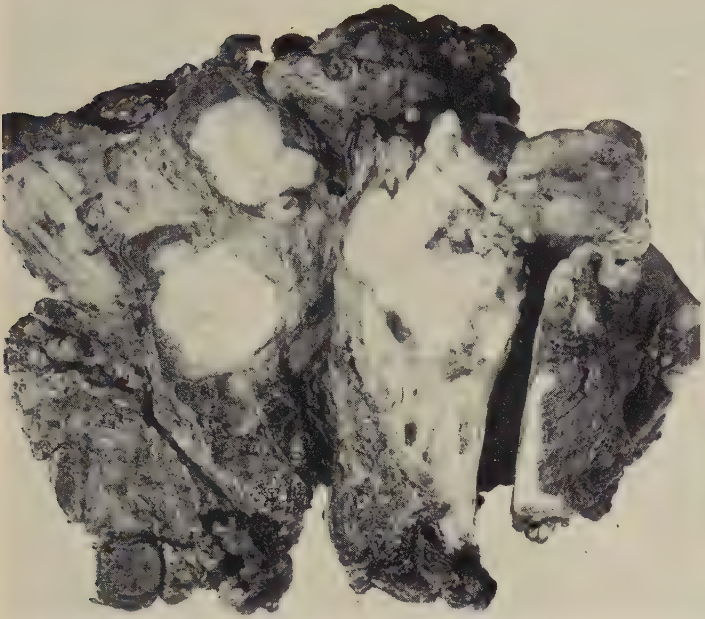
Well differentiated epidermoid carcinoma at base of epiglottis. Details of case at *upper left*. *Left:* histologic anatomy and relationship of the base of the tongue and epiglottis, with tumor at the base of its laryngeal surface. The base of the tongue contains numerous mucous glands; a lingual tonsil projects from its surface into the vallecula. Note loose subepithelial tissue of lingual surface of epiglottis. Fatty tissue of preepiglottic space at lower right. x8. *Right:* keratinizing carcinoma extends to the perichondrium. x31.



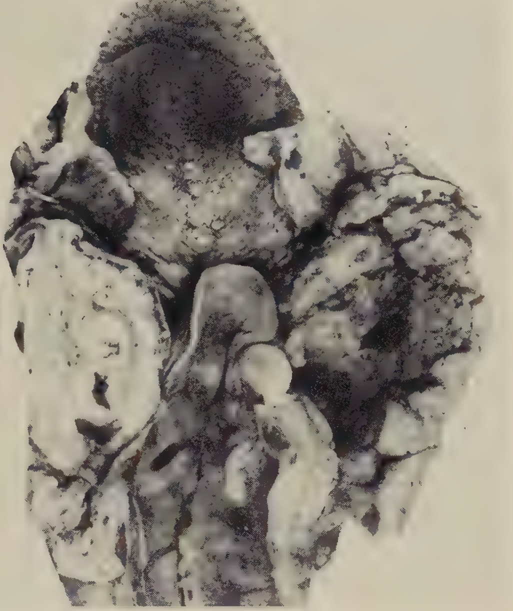
Unilateral radical neck dissection and laryngectomy specimen, including part of hypopharynx. Well differentiated epidermoid carcinoma, primary in hypopharynx, with extensive invasion of larynx and metastasis to one left cervical lymph node. A 56 year old man with dysphagia and enlarging mass in left side of neck for six weeks, and progressive hoarseness for four weeks prior to hospitalization. Operation three months later. *Left:* section through left anterior larynx showing invasion and destruction of the thyroid cartilage and a large defect 8x4 cm. between hypopharynx and larynx at left. *Right:* oblique longitudinal section through left side of specimen showing larger mass of primary tumor (center and left) and invasion of thyroid gland below. (H. Gordon, Louisville, Ky.)



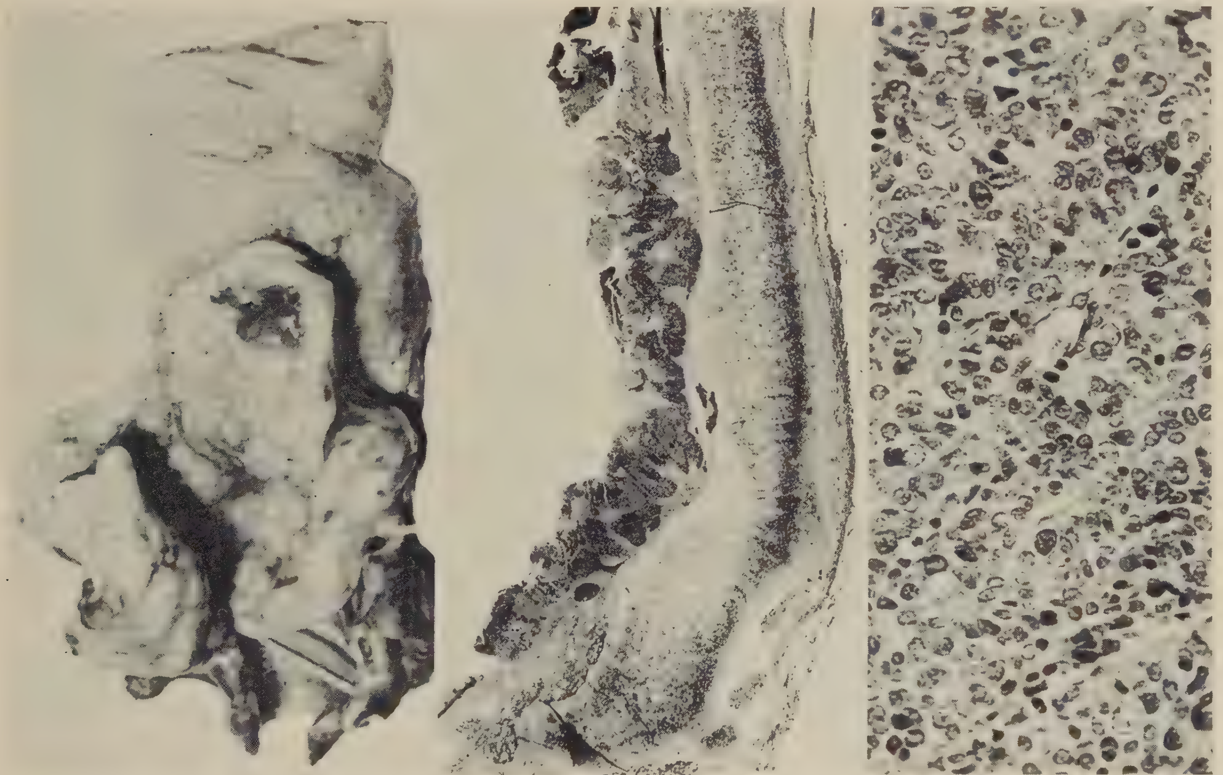
Bilateral radical neck dissection and laryngectomy specimen, including hypopharynx, of 60 year old man with dysphagia for four months, a lump in right neck for two weeks, and a lump in left neck for two days. *Left:* primary carcinoma of the posterior hypopharynx extends to but does not invade the larynx. Cervical lymph node metastases on right and left. *Right:* poorly differentiated adenocarcinoma. Suggestive glandular structure in occasional field as above. x55. No distant metastasis or recurrence several months after operation. (H. Gordon, Louisville, Ky.)



Squamous cell carcinoma, primary in left pyriform fossa, encircling larynx and metastasizing to left cervical nodes. From a 52 year old colored man with dysphagia and hoarseness for several months and hemoptysis for several days. Patient survived several months after operation. (H. Gordon, Louisville).



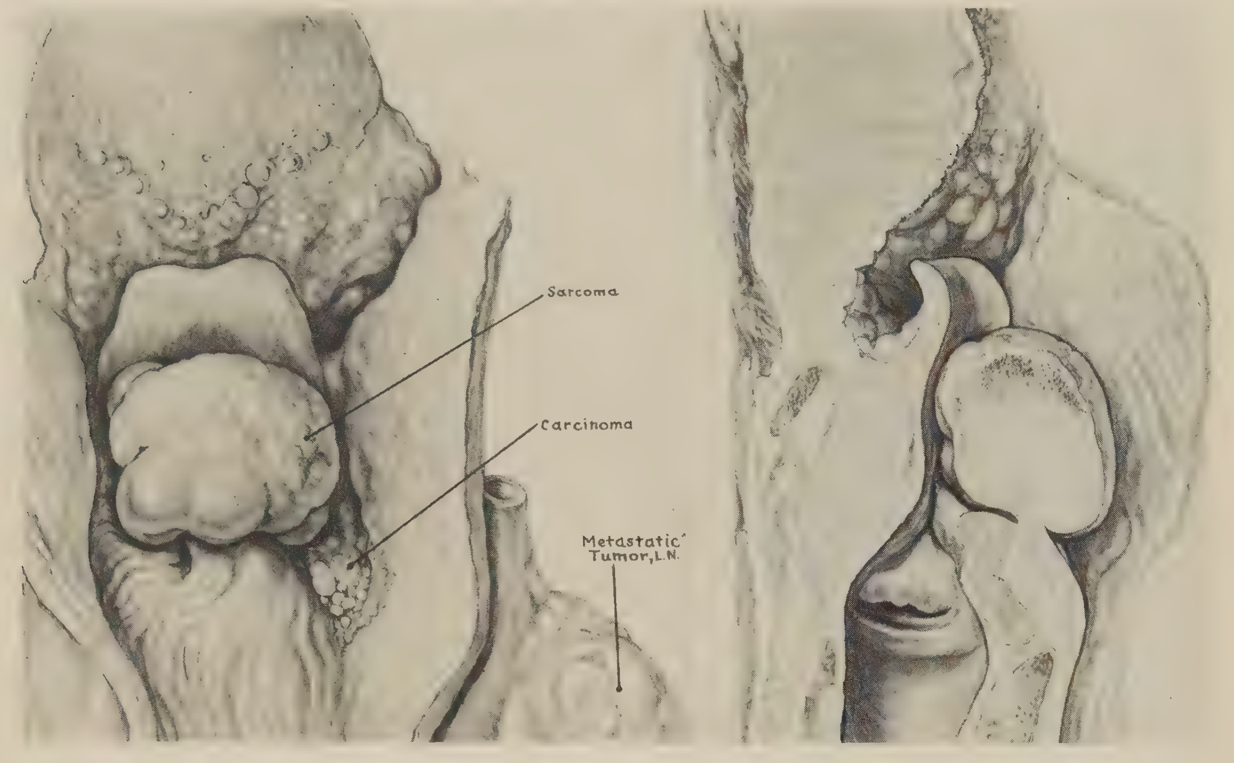
Massive squamous cell carcinoma of hypopharynx involving pyriform fossa and invading larynx. From a 48 year old colored man, who died of pneumonia. Only metastasis was to right submental lymph nodes.



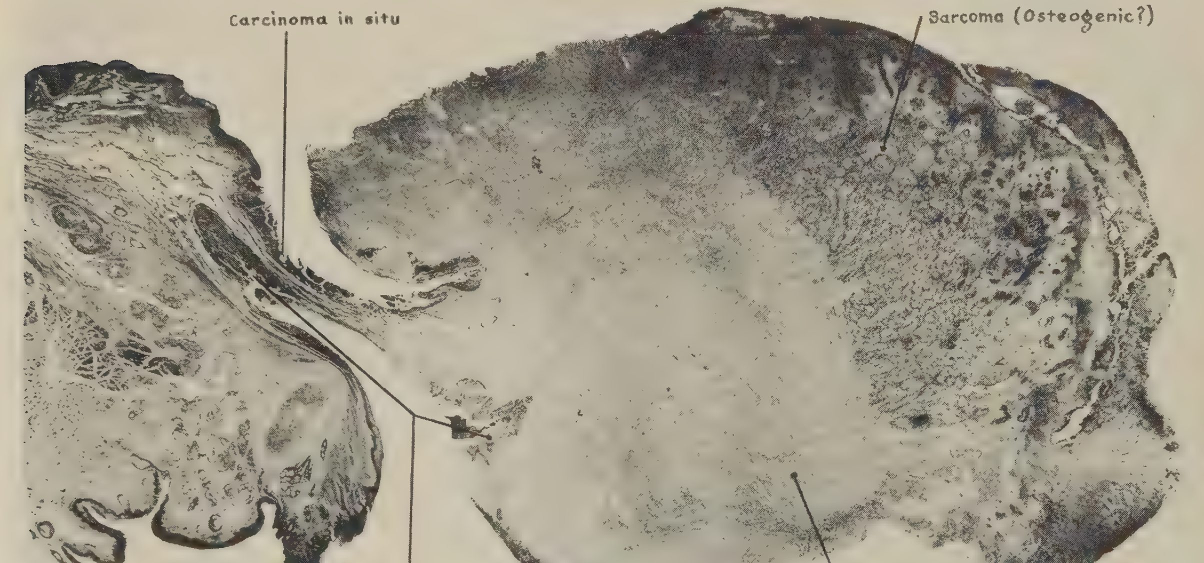
A. Extensive involvement of base of tongue, epiglottis (ulcerated), larynx, upper esophagus and pyriform fossae by a primary **"lymphoepithelioma"** of nasopharynx. Specimen removed at autopsy. Treated two years previously by x-ray and radon seeds. Metastasis only to cervical lymph nodes. B and C. Poorly differentiated **squamatoid carcinoma,** primary in epiglottis of 59 year old white man. It extended to the hypopharynx and esophagus. x 8 and x 330.

CARCINOMA AND SARCOMA, HYPOPHARYNX

("COLLISION TUMOR")

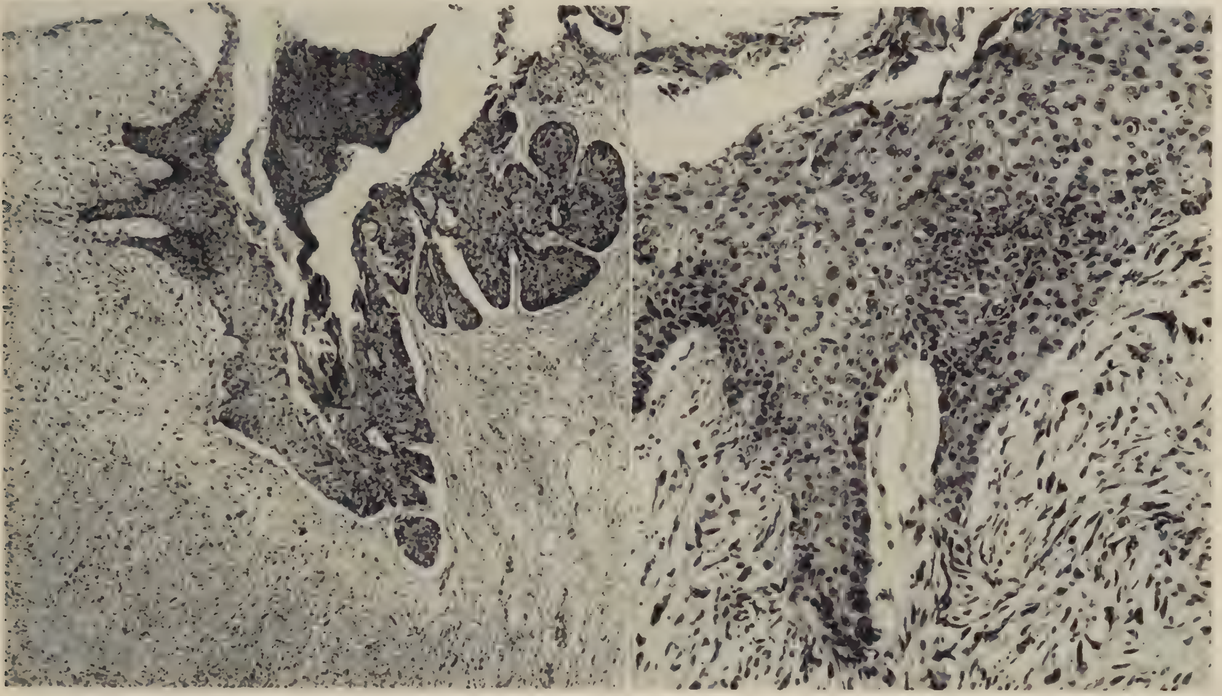

Sarcoma
Carcinoma
Metastatic Tumor, L.N.

Drawings of posterior and lateral views of autopsy specimen. Massive pedunculated sarcoma of right aryepiglottic fold and infiltrating epidermoid carcinoma of right medial and lateral hypopharyngeal walls. 59 year old man with severe dysphagia, pain and hoarseness for three weeks. Epidermoid carcinoma in first biopsy; osteogenic sarcoma as well as carcinoma in second biopsy a few days later. Main tumor surgically removed. Found dead on park bench two months later.

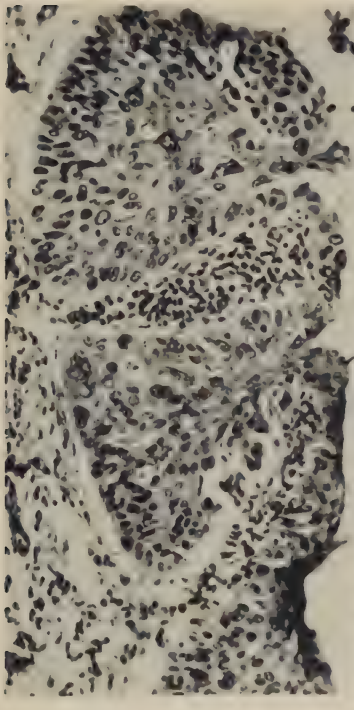

Carcinoma in situ
Sarcoma (Osteogenic?)
Infiltrating Carcinoma
Sarcoma (Fibro)

Low power photomicrograph of the pedunculated mass demonstrates its structural features, and its relationship to hypopharyngeal mucosa and the altered hypopharyngeal epithelium. x6. (Cytologic features, next plate.)

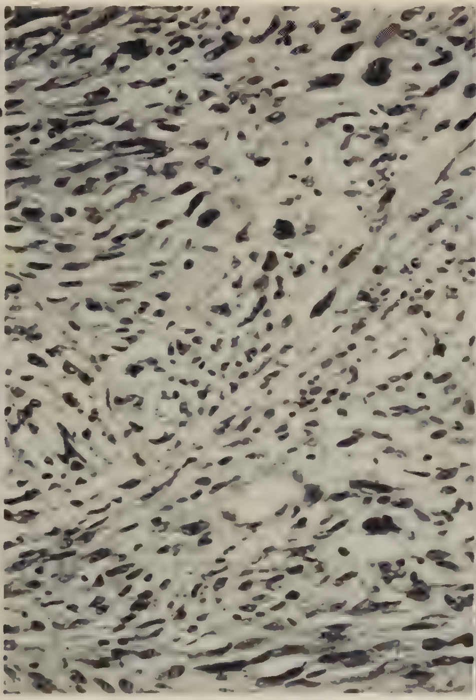
(Drawings and slides, courtesy of A.A. Liebow, New Haven, Conn.)



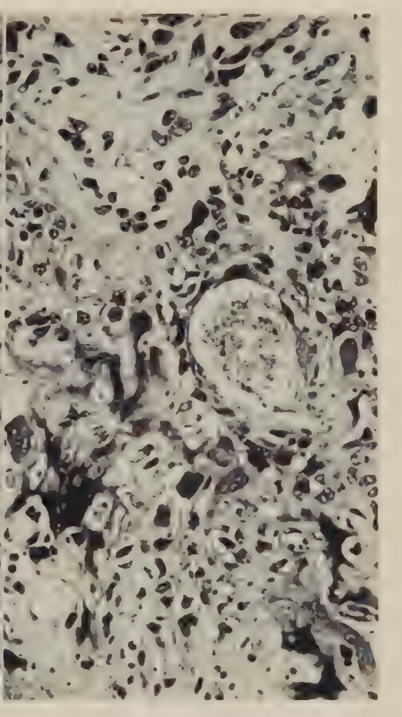
Sarcoma adjacent to invasive carcinoma, both apparently well differentiated. *Left:* base of pedunculated tumor shown on previous plate. x30. *Right:* magnified field from top left of preceding illustration. Intimate relationship of epithelial pegs and underlying fibrosarcoma. x150. (A.A. Liebow, New Haven, Conn.)



"Carcinoma in situ" of adjacent epithelium of hypopharynx and proximal esophagus. x120.

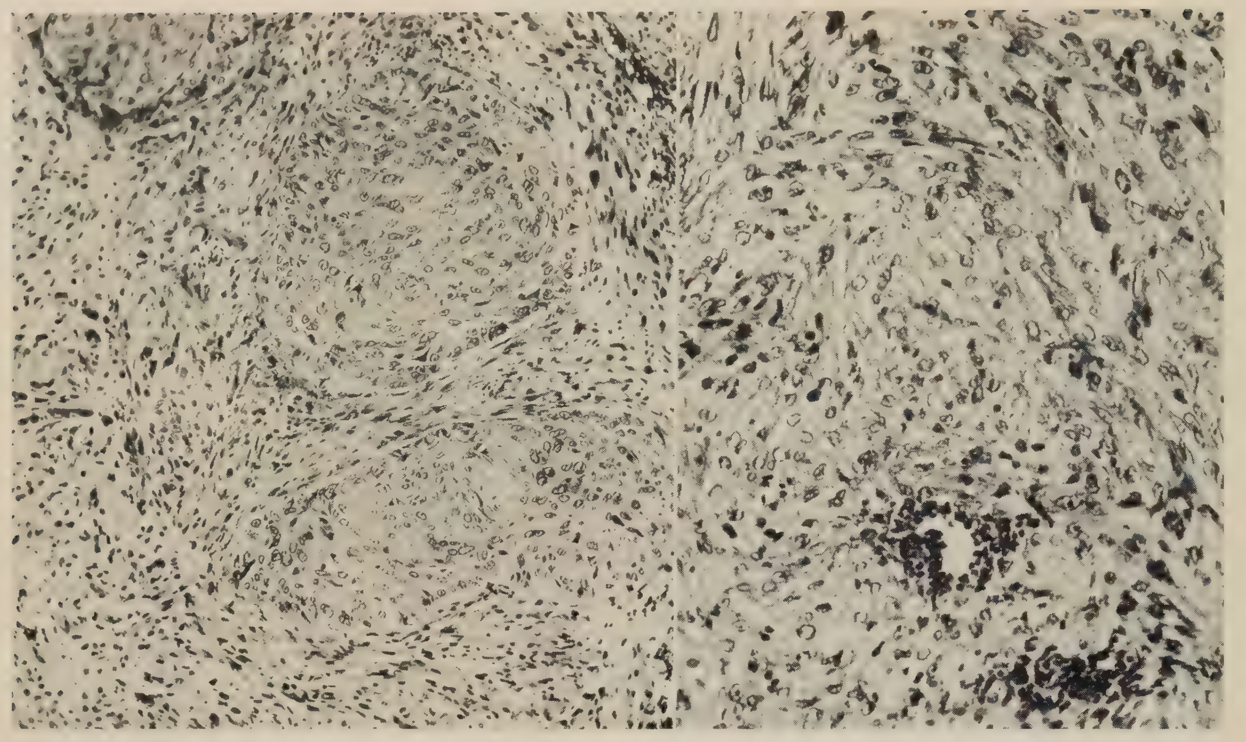


Spindle cell sarcoma in bulk of pedunculated tumor. Some atypical nuclei; frequent mitoses. Abundant collagen demonstrated. x215.

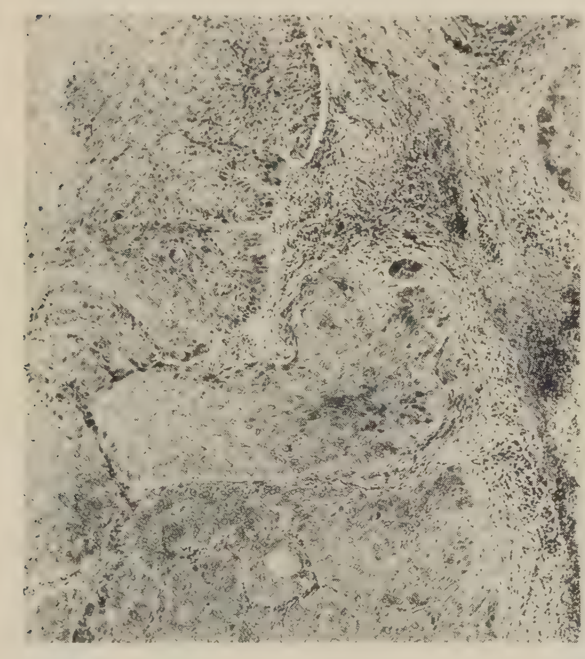


Atypical osteogenesis in peripheral part of tumor, interpreted as osteogenic sarcoma by many. x130.

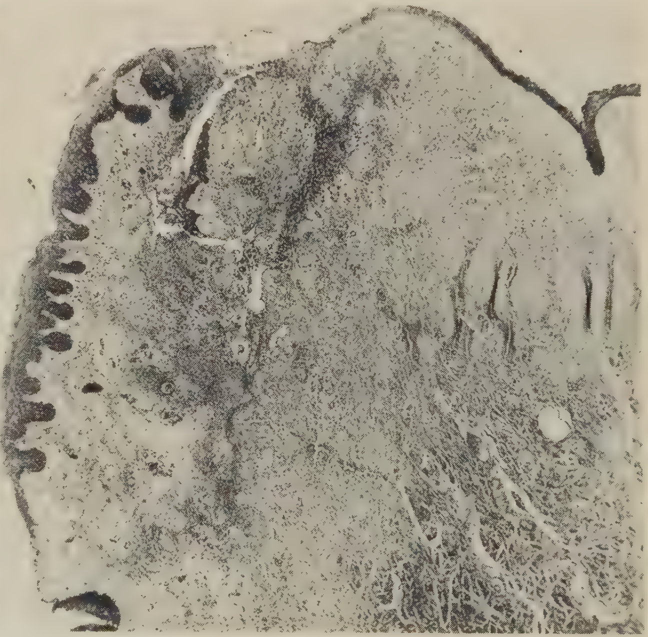
Within a metastatic mass in the upper cervical region were demonstrated separate nodules of well differentiated metastatic carcinoma and metastatic spindle cell sarcoma with osteogenesis.



Cytologic features of "carcinosarcoma" were present in a large pedunculated tumor resected from the larynx of a 56 year old man. *Left:* representative field from central portion of the mass. Islands of well differentiated epidermoid carcinoma surrounded by well differentiated fibrosarcoma producing stainable collagen. Frequent mitoses; occasional atypical and bizarre cells in both elements. x125. *Right:* an occasional field in the predominant sarcoma might be interpreted by some as spindle cell carcinoma. x235.

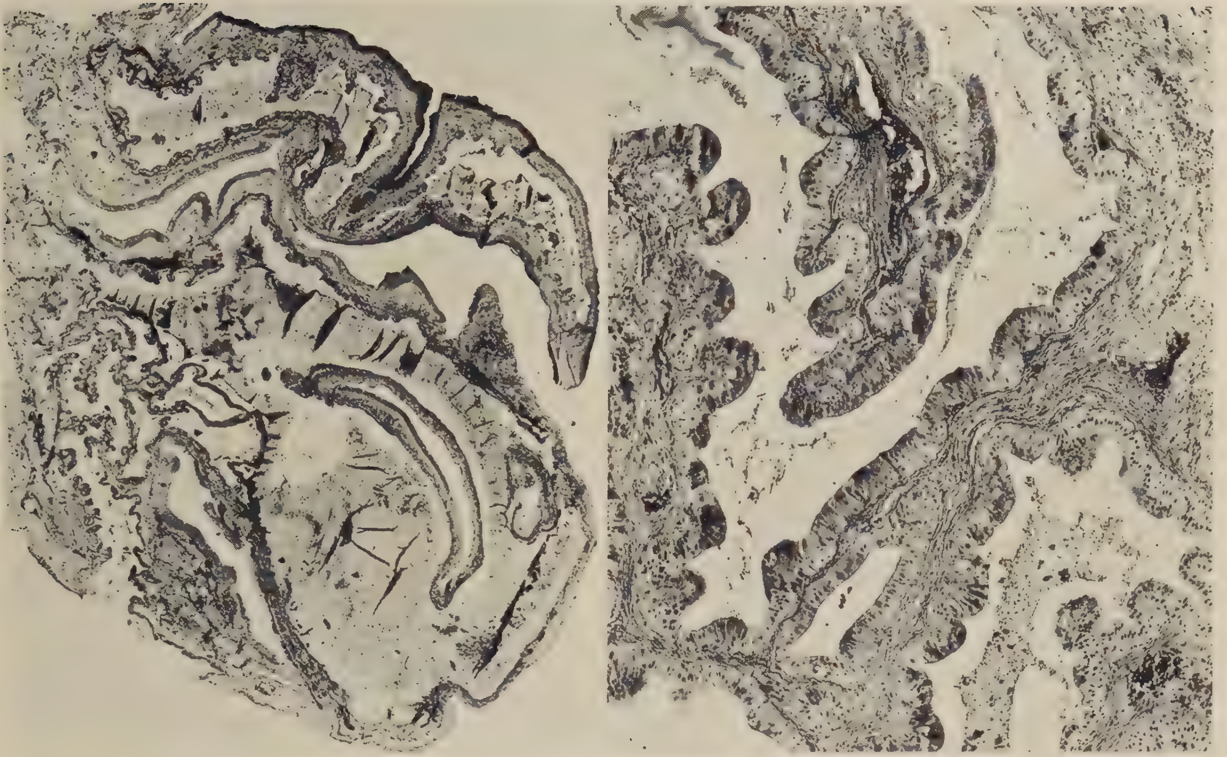


Well differentiated carcinoma without sarcomatous element in only one small area at margin of mass. x70. (P. Kimmelstiel, Charlotte, N.C.)

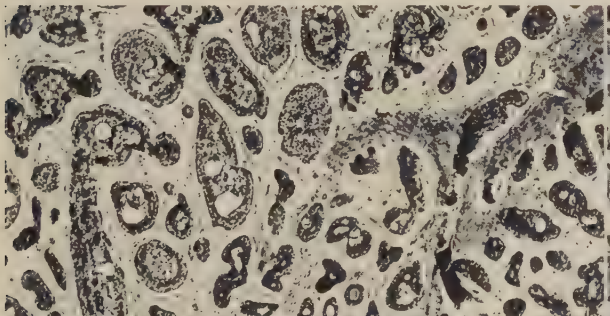


Subsequent laryngectomy specimen contained no residual tumor; only area of leukoplakia and traumatic defect with epithelization and chronic inflammation of one true cord. x40.

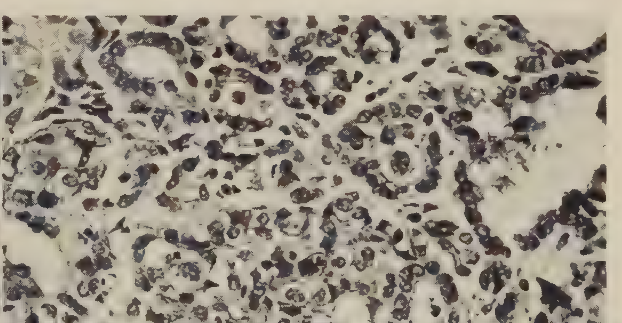
The term carcinosarcoma implies the simultaneous neoplastic growth of the epithelial component of a tissue and its stroma. It should not be confused with the "collision tumor," in which two separate but contiguous tumors develop and there is invasion of one by the other.



Papillary cystadenoma, a very rare type in the larynx, from a 58 year old man with hoarseness for three months. The epithelium, tall columnar with eosinophilic cytoplasm and double row of nuclei, is reminiscent of that commonly seen in Warthin's tumor. Probable origin from ducts of laryngeal glands. x10, x75. (M.L. Barnes, Louisville, Ky.)



Adenoid cystic carcinoma ("cylindroma") deeply infiltrating laryngeal soft tissues. From hemilaryngectomy (followed by deep roentgenotherapy) performed on 40 year old man with hoarseness for two years. x55. Bilateral lung metastasis evident, 10 years after onset. (J.A. Murtagh and R.K. House, Hanover, N.H.)



Adenocarcinoma, base of epiglottis, from 37 year old man with hoarseness for three months. Well differentiated glandular structures in portions of the tumor, though many areas were solidly cellular. x62. Metastatic nodule in skin of chest, with similar histologic pattern, removed three years later.

CHAPTER 26

TRACHEA, BRONCHI, AND LUNGS

TRACHEA

The trachea shares to a certain extent in the inflammatory processes of the larynx and, with the latter, is at times especially susceptible to the common cold. Such specific inflammations as diphtheria and scleroma may extend to the trachea, but there are no additional pathologic features of the diseases in this location, although they may produce serious constriction of the trachea.

Holinger and associates have recently reviewed the subject of **benign stenosis** of the trachea including that due to congenital anomalies and acquired lesions. They classify the congenital anomalies as follows:

Webs—congenital hour-glass constriction
Fibrous stricture of a segment of trachea
Stenosis associated with congenital atresia and tracheo-esophageal fistula
Stenosis due to absence or deformity of tracheal cartilages
Tracheomalacia
Cartilaginous deformity
Stenosis associated with vascular ring

The last anomaly has become of more importance since the advances in cardiovascular surgery have made it amenable to correction. Edwards recently published a comprehensive review of the embryology of the defect and its different manifestations.

A rare type of ossification affecting the trachea, bronchi and lungs is called TRACHEOPATHIA OSTEOPLASTICA. It consists of multiple nodules of bone and cartilage that usually grow between the cartilaginous rings and just under the mucosa.

Primary tumors of the trachea are rare, the most frequent being carcinoma which tends to occur at the bifurcation. The trachea is frequently invaded by carcinoma of the esophagus and of the thyroid gland. Holinger and associates recently reported twenty-eight cases, eighteen of which were primary in the trachea. The authors emphasize the clinical point that these tumors seldom become manifest before they have caused respiratory embarrassment.

BENIGN PAPILLOMAS may develop in the trachea and BENIGN ADENOMAS of the gland elements occur occasionally. The trachea may also be the seat of a rare bronchial adenoma. Holley, in his review of the thirty-nine cases in the Registry, reported none from the trachea, but the over-all experience indicates that it may occur anywhere along the respiratory tract.

Dean reviewed the history and classification of tumors of the trachea that present adenomatous or adenoid features. As a result he concluded that CARCINOMA of the trachea is relatively rare but that its incidence appears to be increasing. Carcinoma occurs in about equal proportions as squamous cell and adenomatous types. The incidence of metastasis in the squamous cell carcinoma is much higher than in the adenomatous. Krompecher's theory is that some basilar cells of the respiratory epithelium are not completely differentiated and retain a potentiality for differentiation to squamous, glandular, or columnar type.

Adenocarcinoma may give a long history of symptoms. It has been the experience of some that adenocarcinoma of the lower half of the trachea is invariably fatal, while that occurring in the upper half is more amenable to local removal. It is likely that the basaloid adenocystic bronchial adenoma and the mixed tumor of the salivary-gland type are included in this category. Recently, surgical resection of the trachea has been accomplished, providing a therapeutic approach previously considered impossible.

BRONCHI

It is not necessary for our purposes to go into the minutiae of bronchial pathology, but only to include those conditions that are of interest to the bronchoscopist, and even of these, we can exclude foreign bodies. Five topics will be stressed: bronchiectasis, asthma, bronchogenic carcinoma, bronchial adenoma, and pulmonary adenomatosis.

Bronchiectasis is the permanent dilatation of a bronchus. There are several factors involved in its pathogenesis. The most obvious is the obstruction of a bronchus by tumor, an enlarged lymph node, a foreign body, or an inspissated mucous plug. The commonest cause, however, is an inflammatory process that so alters the bronchial structure that the ciliated epithelium can no longer function, and that destroys the elastic and muscular elements of the wall, leading to dilatation. Both factors favor the accumulation of mucus, exudate, and infection. There is always atelectasis and fibrosis of the surrounding parenchyma, and the drag from the latter adds further to the dilatation. The importance of inflammation over simple obstruction is indicated by the fact that the basis for the great majority of the cases is laid in lung infections during childhood, a factor that, according to Holinger, is too often overlooked. In this connection, it is necessary to exclude from the category of true bronchiectasis the congenital cyst resulting from atresia of a bronchus. There is practically always a history of a respiratory difficulty some years preceding the development of the recognizable lesion, and this is usually the history of a childhood pulmonary episode.

Bronchiectasis may be either of the true or false type. The former is a primary dilatation of a bronchus with retention of the wall structure, including more or less of its lining epithelium. In the false, the cavity is produced primarily by the dilatation of the bronchus, but it is enlarged by erosion of the wall and contiguous lung tissue. When the contents are purulent it might more properly be termed pulmonary abscess.

Congenital bronchiectasis in embryos without evidence of inflammation or bronchial obstruction has been reported by Altmann. Through anaplasia of lung parenchyma there is decrease in resistance to the bronchial expansion and such a lesion might be interpreted more properly as a developmental defect than as orthodox bronchiectasis.

Cavities occasionally develop about inhaled foreign bodies. This can be taken as an example of the false type of bronchiectasis. It is illustrated in the following plates. The patient inhaled pine needles and pneumonia developed four months later. The left lower lobe was removed after an additional two months. It was atelectatic and contained several bronchiectatic cavities. The pine needles were readily identified.

The relationship of chronic sinus disease to bronchiectasis is not clearly established in spite of the fact that they are so frequently associated. There seems little question, however, that sinus disease can be at least a contributory and sustaining factor, particularly when it occurs as the hyperplastic type of rhinitis and sinusitis. The mucosa in this type of inflammation is inadequate physiologically, and it is the seat of continued infection that can interfere with drainage and aeration of the nose and sinuses.

The role of infection in the production of the lesion is not always evident in the established cavity. The contraction of scar tissue in the peribronchial tissues might be included as a possible etiologic factor and its development is very likely influenced by the primary atelectasis of the surrounding lung parenchyma. Generally more than one bronchus of a given area of the lung is involved.

The lesion is most common in the dorso-medial portions of the lower lobes and in the left lung more frequently than in the right. The cavities may be saccular or fusiform, but are more commonly cylindrical. They are surrounded by more or less atelectatic lung tissue and fibrosis, but when smaller bronchi are involved the cavities sometimes reach the pleural surface. The contents are usually tenacious, grumous mucus or purulent material. Histologically, the walls of the involved bronchi are thick, hyperemic, and there is definite abscess formation. Ulceration of the epithelial mucosa is undoubtedly present in the early stages, but repair of the epithelium is actively carried out. The epithelium may change in character either to squamous or to the more columnar mucoid type. There is usually more or less replacement of the cartilaginous and muscular elements of the wall by scar tissue.

Bronchial Asthma.—The discussion will be limited to the true spasmodic asthma that is on an allergic basis. The features of the early phase depend on exposure to the sensitizing antigens. In this stage the process is reversible by the avoidance of such exposure or by immunizing therapy.

Bacterial infections in the respiratory tract and viral diseases, such as measles, may be associated with asthmatic bronchitis. The acute paroxysms are more severe at the onset of a viral infection, then subside, but return later with increased severity. The asthma persists throughout a bacterial infection when the patient is hypersensitive to the particular bacterium involved. Focal infection is a definite factor in the development of asthma at any age. As in all allergic states, the hereditary background is important.

The clinical episode is due to spasm of the smooth muscle of the smaller bronchi resulting in difficulty in expiration. The later effects are irreversible. These consist of emphysema, hyperplasia of the bronchial muscularis, more or less plugging of the bronchioles and smaller bronchi with tenacious mucus, and marked increase in mucus secretion by the lining cells. The larger bronchi are usually not involved.

Histologically, the picture is characterized by the over-distended air alveoli with rupture of the walls; the presence of chronic exudate in, and fibrosis of the bronchial walls; hypertrophy of the mucous glands with manifest hypersecretory activity; hyperplasia of the bronchial muscularis; hyaline thickening of the mucosal basement membrane, similar to that seen in the chronic allergic reactions in the nasal and sinus mucosae; hyperplasia of the epithelial mucosa including plications and the presence of goblet cells, and the mucous plugs containing desquamated epithelium and an eosinophilic exudate in the bronchial lumens.

In such conditions as bronchiectasis and asthma when there is destruction of bronchial tissue, the mucous pearls of Laennec, Charcot-Leyden crystals, and Curschmann spirals may be found in the sputum. Before x-ray was available as a diagnostic aid, these items were considered of great importance.

Fungus infections of the lungs are discussed and illustrated in Chapter 11.

BRONCHIAL TUMORS

Benign tumors of the bronchi are rare. An occasional adenoma developing from the bronchial mucous glands, papilloma of the mucosa, and the still rarer benign chondroma of bronchial cartilage are the only ones of significance. The chondroma is usually referred to as a hamartoma on the assumption that it is a developmental defect rather than a true neoplasm. Although predominantly of cartilage, it contains other elements of the bronchus. It is usually symptomless and discovered incidentally on x-ray examination. Moersch, Donoghue and McDonald recently reported a study of 35 cases. There were twice as many males as females in their series. The chondromas were located in various parts of the lung and in none was there indication of malignancy.

The lung cyst is of clinical importance, particularly the surface air bulla that may be either congenital or acquired. Such a lesion can be the source of spontaneous pneumothorax or, when it ruptures into the mediastinum, can be responsible for the syndrome of pain and peculiar subjective and objective noises typical of that accident.

Bronchogenic carcinoma.—There is still dispute as to whether primary carcinoma arises from other than bronchial epithelium, but this dispute need not concern us here because we are dealing only with tumors that present in the bronchi.

Evidence indicates that there has been an actual increase in the incidence of lung cancer in the last two decades. Attempts have been made to explain this as a consequence of the greater prevalence of cigarette smoking and the presence of possible carcinogenic substances in the atmosphere—coal smoke and volatile substances in paving materials, for example. There is no doubt about the influence of certain chemicals, the classic examples being the high incidence of lung carçinoma among mine workers, particularly the cobalt miners in Schneeberg, Germany. The presence of radioactive dust in these mines rather than the specific mineral is now considered the important factor.

There is a significant difference in the distribution of tumors because of sex and age. Bronchogenic carcinoma occurs from three to ten times more frequently in males (depending on whose statistics one sees) and most commonly after the fourth decade. Bronchial adenoma, on the other hand, is more frequent in the female and at an earlier age.

Carcinoma occurs more frequently in the bronchus to the upper right lobe than in the other bronchi. It is uncommon in the right middle lobe. It may arise in the main bronchus to a lobe or at the bifurcation of the trachea. It is predominantly a tumor of the large bronchi, but an origin in more peripheral portions of the lungs is not uncommon. In tumors of portions of the bronchial tree that are inaccessible to bronchoscopy, the Papanicolaou technique becomes an important adjunct in the diagnosis, since it is possible to identify tumor cells in the sputum and in bronchial washings.

The tumor may present as a papillary projection of the mucosal surface, as a sessile or even less evident inflammation of the bronchial wall. The bronchoscopist has to differentiate between neoplastic and inflammatory lesions and this will be difficult without biopsy. The necessity for obtaining adequately representative material for diagnosis is obvious.

Grossly, the tumor in most instances appears as a grayish white mass, partially or completely surrounding the lumen of the involved bronchus. There may be diffusion through the surrounding parenchyma, erosion of bronchial mucosa, and projection of a rough surfaced or papillary mass into the lumen. If the tumor has caused obstruction of the bronchus, the associated parenchyma will be atelectatic and the bronchial outlines accentuated by increased white fibrous tissue, or frank bronchiectasis will have resulted in the distal portions of the bronchial tree. Secondary nodules of tumor may be present in the adjacent or more distant lung parenchyma.

Microscopically, the cell type is most variable, not only in different tumors but in different portions of an individual tumor and its metastases. Most of the tumors, however, can be classified in relation to one of three cell types: squamous cell (epidermoid), glandular (adenocarcinoma), and small (oat cell) undifferentiated or anaplastic cell. There is a certain amount of practical significance in this classification, because the anaplastic tumors tend to metastasize much more readily than the others. This type is found most frequently in main stem bronchi. The cells are small, fairly uniformly spindle shaped, and are indiscriminately grouped in small and larger masses that are free of stroma. In some instances this tumor will extend widely through the contiguous lung parenchyma and exist for a long time without metastasis.

Squamous cell carcinoma occurs most commonly in the lobular bronchi. It is made up, all or in part, of cells of the epidermal type that may even show intercellular prickles and typical cancer pearls. When the tumor is more rapidly growing, much of it is made up of strands and nests of less differentiated cells. The adenocarcinoma arises from cells of the mucosal glands and possibly from the surface cells that have potentiality for mucus production. The cells of the tumor are cuboidal rather than columnar in shape and show a definite tendency to acinar arrangement and more or less mucus-production activity. Smetana and associates included twenty-two cases of adenocarcinoma in their analysis of 100 bronchogenic carcinomas. There was metastasis in all of the twenty-two.

The commonest site of metastasis of lung carcinoma is to the hilar or mediastinal lymph nodes. An early sign may be the involvement of the supraclavicular or axillary nodes. The propensity for metastasis to the brain, adrenals, and bones is evident in the general history of the tumor.

Pancoast tumor.—Mention should be made of the clinical entity, first described by Pancoast, that results from the presence of malignant tumor in the superior pulmonary sulcus. Involvement of the brachial and cervical sympathetic nerve plexuses produces ptosis, mydriasis, anhidrosis, and flushing of the face on the affected side. This is Horner's syndrome. The tumor is not a special entity histologically as was originally considered. It is most commonly an extension of bronchogenic carcinoma through the apex of the lung.

Bronchial adenoma has such special clinical features and histologic characteristics that it is necessary to separate it from frank bronchogenic carcinoma. The term adenoma is not entirely correct because, in the first place, the tumor is not always of adenomatous structure, and, in the second place, a considerable percentage of the tumors prove to be malignant by persistent invasion and, less frequently, by distant metastasis. The initial clinical differences are that they are more common in the female than in the male and that they occur in a somewhat younger age group than do the frank carcinomas. It is not uncommon for metastasis to occur years after the recognition of the primary tumor.

The tumor occurs most commonly in the larger bronchi near the hilum of the lung; it is either sessile or pedunculated and rarely shows ulceration. Grossly, it gives the impression of being a circumscribed growth, but it does infiltrate in the submucosal tissue and even beyond the limits of the bronchial wall into the surrounding parenchyma. The frequency with which it penetrates the bronchial wall and expands in the adjacent tissue has led to the designation "dumb-bell tumor." This characteristic is responsible for the failure to eradicate the tumor by removing the portion available through a bronchoscope.

It is considered by some that the bronchial adenoma is histogenetically and clinically closely related to the mixed tumor of the salivary gland type. There are the same complicated cell characteristics, but not the consistent content of mesenchymal elements as in the more classically localized tumors of the salivary glands. Liebow insists that these tumors do not resemble the salivary gland mixed tumor and that the mesenchymal elements that are seen in them are those appropriated from, or resulting from metaplasia of local tissues. There is no disputing the fact, however, that the cylindromatous feature and the basaloid adenocystic type are common to both. Clinically, they are similar in that they do not recur and invade, but they infrequently metastasize and then only after a very long time. The variation in the histologic picture from undifferentiated spindle basaloid cells to well differentiated columnar gland elements and to squamous cells is responsible for the large group of names. In addition to mixed tumor, it has been called basaloid carcinoma, carcinoid, and cylindroma, to mention a few of the synonyms.

Tumors identical to those arising in the bronchi occur along the trachea, in the lungs, and very occasionally in the upper respiratory tract. An instance of its development in the epiglottis will be seen in the illustrations.

There is also wide variation in the arrangement of the cells. The basaloid cells may show no tendency to adenomatous formation but may be present in diffuse sheets or fascicles, in the latter instance supported by strands of hyalinized stroma. They may show the adenoid quality of the basal cell tumor arising from hair follicles in the skin. The glandular element more commonly shows definite acinar arrangement. Holley, as the result of the study of thirty-nine cases at the Armed Forces Institute of Pathology, was able to identify two histologic types: the first, the carcinoid tumor in which the cells resemble closely those of the intestinal carcinoid; in fact, in several instances he was able to demonstrate argentophil granules in the cells. The second and much smaller group in Holley's series are those in which the mixed-tumor characteristics were fairly evident, including those showing the epithelioma-adenoides-cysticum and cylindroma types of basal cell tumors of the skin. The cylindroma is characterized by the palisading of the basal-type cells along the strands of hyalinized stroma.

While it is not difficult to assign bronchial adenomas to one or another of the two groups, there is a question as to whether it should imply that there is a difference in the histogenesis. One argument for considering the bronchial adenomas very close histogenetically to mixed tumors of the salivary glands, and certain basaloid tumors and mixed tumors of the skin similarly close to adenomatous tumors of the breast and other parts, is that they all arise where there are secreting glands. Whether they develop directly from mature glands is doubtful. They probably arise from embryonal primordia. It is not necessary to revert to such a remote localized origin for the bronchial adenoma as the bronchial bud, as suggested by Graham and Womack.

The bronchial adenoma was formerly considered to be a benign lesion and therefore not to require radical treatment. It is evident now with more material and longer follow-ups that this is not invariable. A number of cases have now been reported in which, in addition to involvement of local lymph nodes, there have been distant metastases, particularly to the liver.

The long interval that usually elapses between the discovery of the primary adenoma and the metastasis is exemplified in a case from the Registry, in which metastasis to the liver was an incidental finding during laparotomy some ten years after lobectomy had been performed for the removal of the primary tumor. The histologic character of the primary tumor and of the metastasis were identical. This is usually the case.

The number of instances in which the tumor has been entirely removed through the bronchoscope is significant. However, if tomograms indicate the likelihood of infiltration beyond the bronchus, if bleeding is excessive, or if visible changes have occurred in the lung beyond the tumor, radical surgery is indicated. With involvement of the main bronchus, bronchotomy may be indicated in an effort to preserve functioning lung. With involvement of a lobar or segmental bronchus, lobectomy or segmental lobectomy may suffice. Total pneumonectomy is indicated if involvement of the main bronchus cannot be relieved by bronchotomy or if the lung distal to the tumor has been destroyed by the obstruction.

Pulmonary adenomatosis (bronchiolar carcinoma, alveolar carcinoma) is a rare and puzzling lesion of the lungs in man that must be separated from the bronchial adenoma on the one hand and the bronchogenic carcinoma on the other. There is considerable confusion as to whether all the cases that are now included in this category are of a similar nature, but certainly some of them have the clinical and pathologic characteristics of the common and economically important lesion that occurs in sheep in some regions, notably Iceland. This is the jaagsiekte of South Africa. This was true of most of the cases that were reported by Swann from the Armed Forces Institute of Pathology. Liebow, however, in his excellent fascicle on "Tumors of the Lower Respiratory Tract" prefers to consider the lesion a carcinoma arising from the bronchiolar epithelium. Among the cases that are now included in the group, about half have exhibited metastasis. According to this interpretation, therefore, the tumor would lie midway, so far as frank malignancy is concerned, between the bronchial adenoma and bronchogenic carcinoma. The question of its histogenesis is not settled. In this connection Liebow has called attention to the metaplasia of bronchiolar epithelium that occurs in chronic fibrosing inflammatory conditions of the lung, and to the similarity of these changes to frankly malignant neoplasm of the lung.

Bronchiolar carcinoma is a very slowly progressing disease of adults, but eventually it is fatal because it is usually bilateral and replaces too much of the physiologically active lung tissue. There is no apparent sex selectivity.

Early symptoms are cough, dyspnea, night sweats and loss of weight, a picture usually suggesting a diagnosis of tuberculosis. Very early cases with localized lesions have been successfuly treated by lobectomy, but the vagueness of the symptoms and unspecific x-ray appearance militate against the adoption of proper measures.

Grossly, the affected portion of the lung is nodular, one or more lobes being affected. The lesions are firm and on section the involved parenchyma shows whitish nodules that may indicate grossly their high mucin content.

Histologically, there is a characteristic replacement of alveolar lining cells by tall columnar cells, usually arranged in a papillary manner, that are active mucin secretors. The bronchi are not involved, but there is considerable fibrosis of the parenchyma.

Primary tumors of the pleura are rare and are of two types, the localized fibroma or fibrosarcoma, usually pedunculated and benign, and a diffuse type that more or less ensheaths the lung. They are both of mesothelial origin.

The lungs are common localizations of **metastatic tumors.** Any tumor that invades the blood vessels is especially likely to be filtered out by the lungs. Sarcomas, therefore, are the commonest metastic tumors, but certain carcinomas frequently lodge there, particularly those of the breast and the hypernephroid tumor of the kidney.

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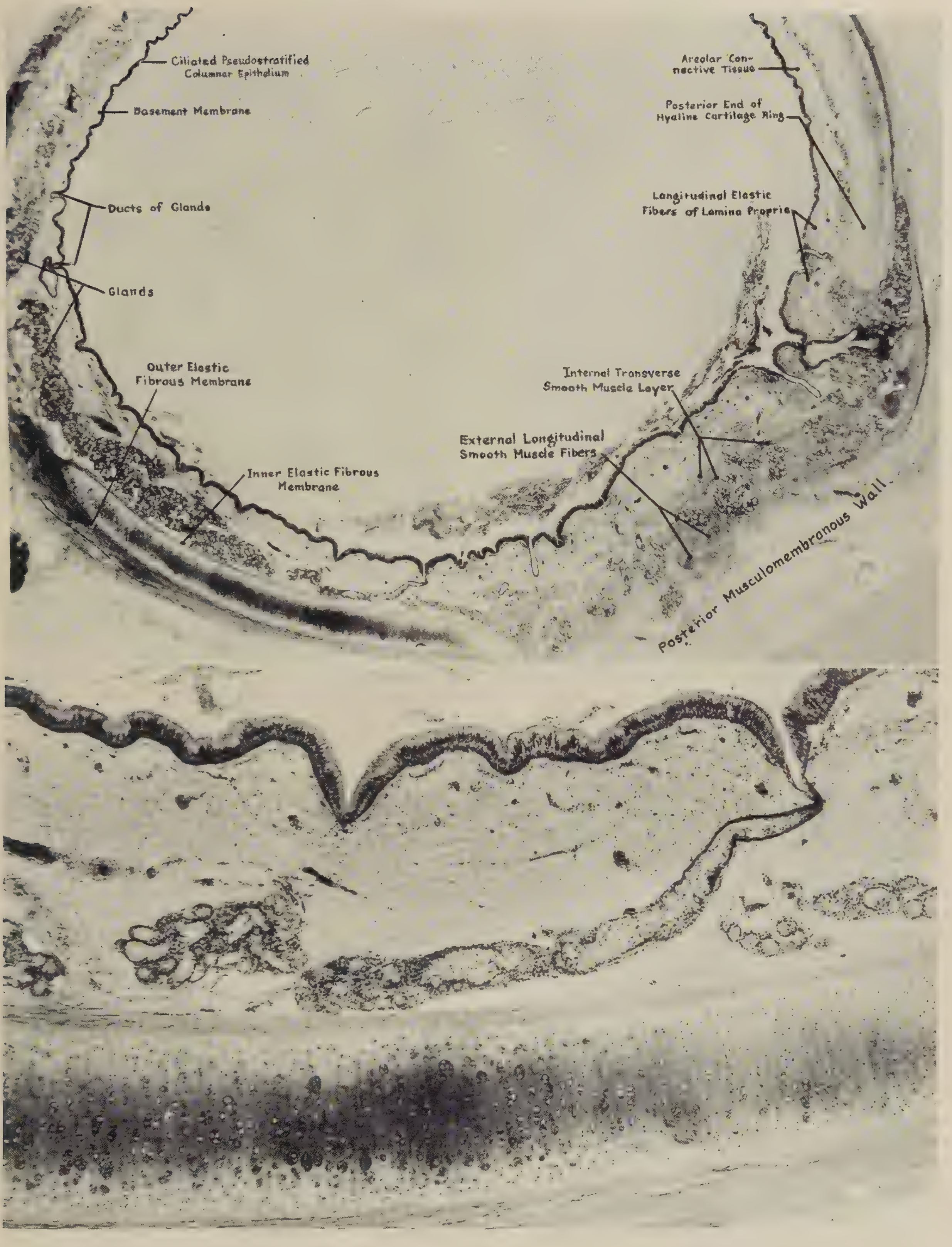
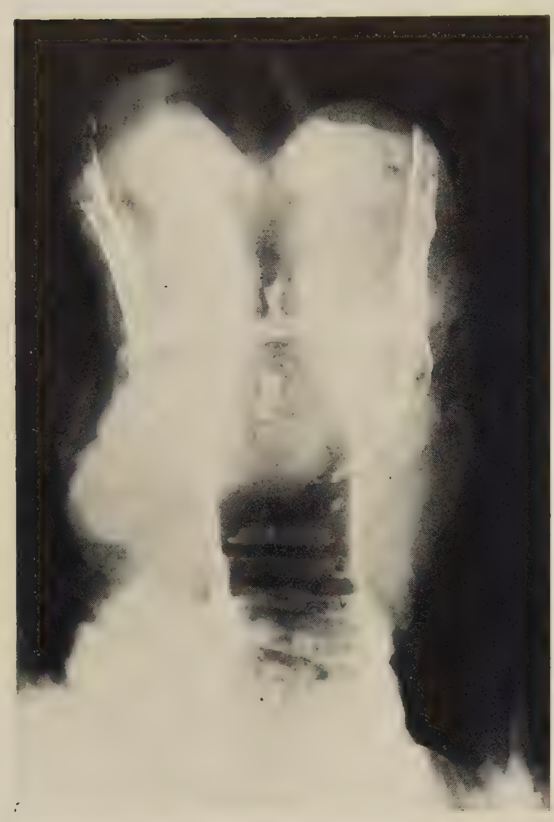

Ciliated Pseudostratified Columnar Epithelium
Basement Membrane
Ducts of Glands
Glands
Outer Elastic Fibrous Membrane
Inner Elastic Fibrous Membrane
Areolar Connective Tissue
Posterior End of Hyaline Cartilage Ring
Longitudinal Elastic Fibers of Lamina Propria
Internal Transverse Smooth Muscle Layer
External Longitudinal Smooth Muscle Fibers
Posterior Musculomembranous Wall

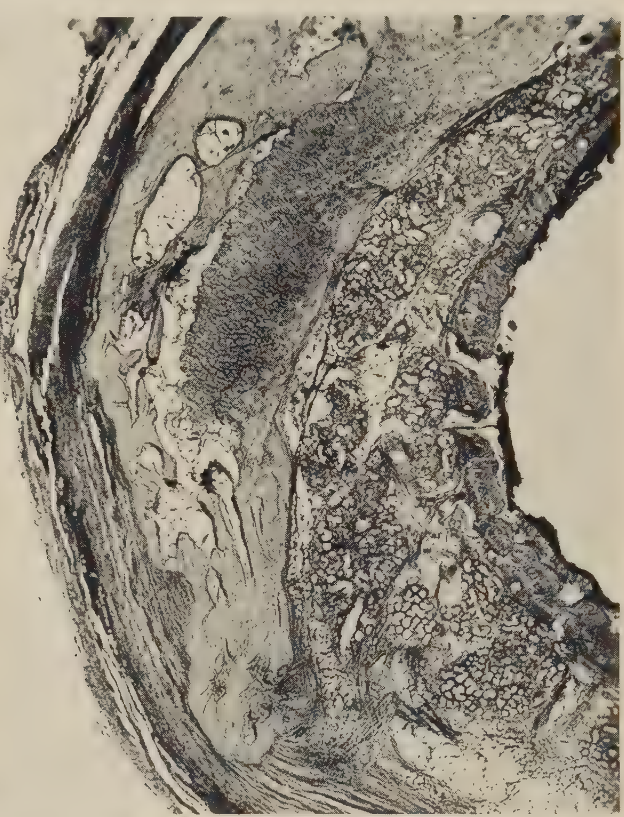
(Upper). Transverse section of trachea through a cartilaginous ring. x10.

(Lower). Histologic detail of a segment of tracheal wall. Note entire glandular duct, including its orifice. x50.

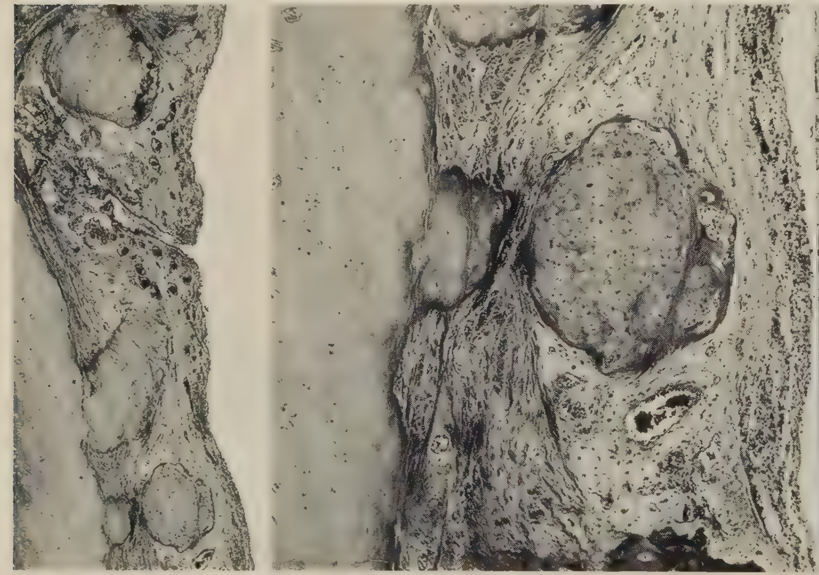
TRACHEOPATHIA OSTEOCHONDROPLASTICA



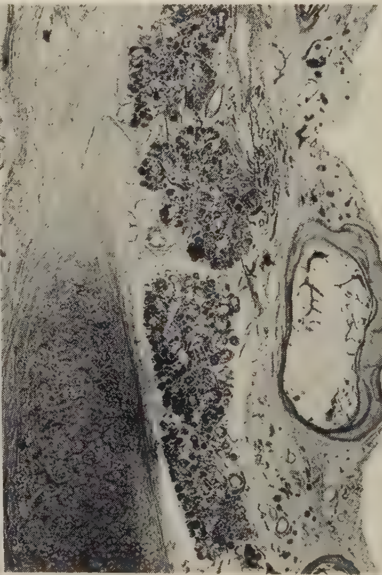
Ossification of thyroid and tracheal cartilages. Outline of cartilages emphasized in the roentgenogram by ossification.



Ossification of tracheal cartilage does not occur as readily as ossification of the thyroid cartilage. Metaplastic bone and fatty marrow at left, remaining cartilage at right. (W. Putschar, Charleston, W.Va.)



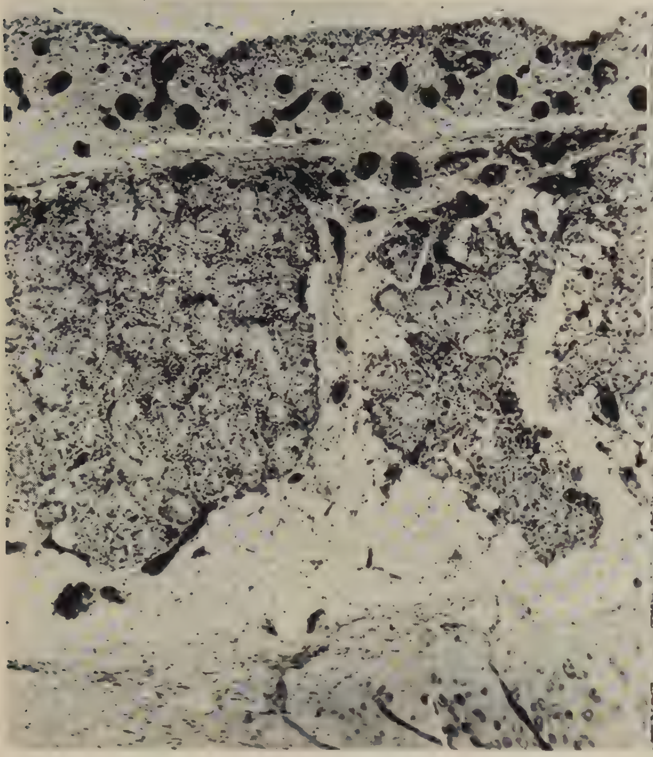
Tracheopathia osteochondroplastica in patient who died of pulmonary and disseminated tuberculosis. Numerous tiny cartilaginous excrescences from tracheal cartilage and free in the mucosa. Metaplastic bone within one (at bottom). x23, x55.



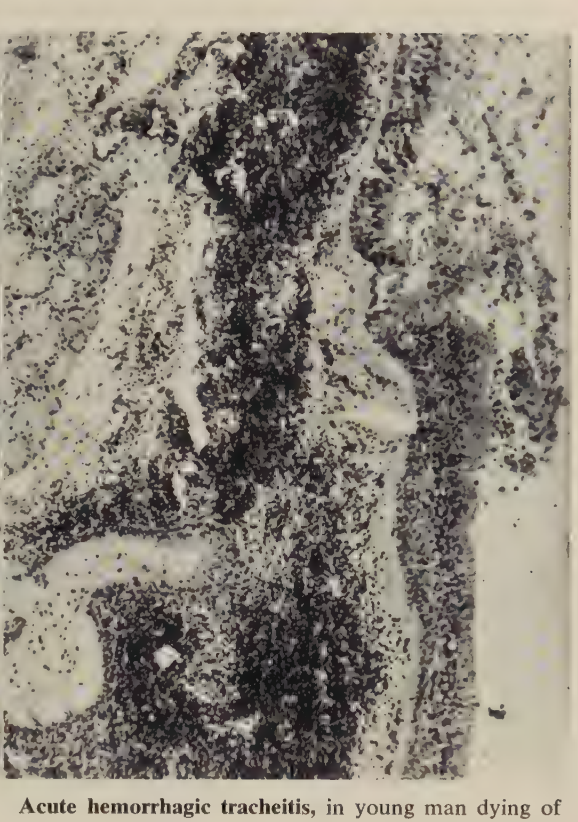
Tracheopathia osteoplastica. Islands of trabeculated bone containing fatty marrow lie free within the mucosa; no apparent connection with tracheal cartilage. x21. (W. Putschar, Charleston.)

ACUTE INFLAMMATION OF TRACHEA

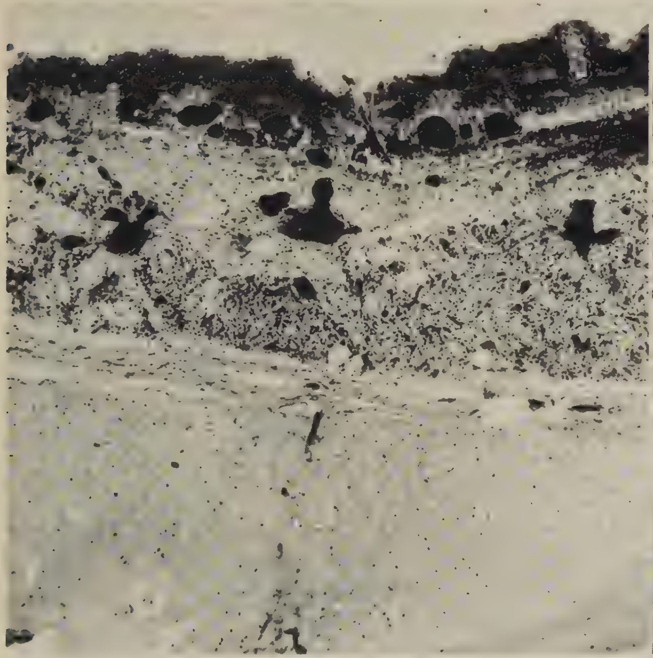
(TRACHEITIS; TRACHEOBRONCHITIS)



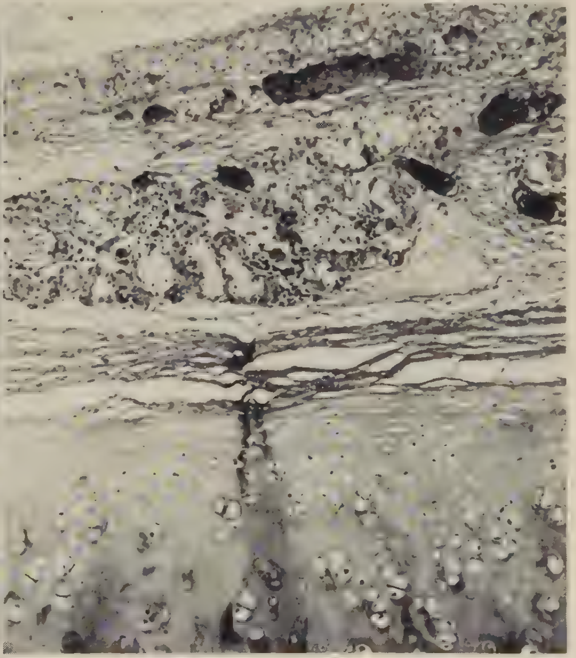
Acute tracheitis in 70 year old patient who died of lobar pneumonia. Erosion of surface epithelium; severe edema of mucosa; marked vascular congestion; prominent subepithelial and periglandular inflammatory exudate. x55.



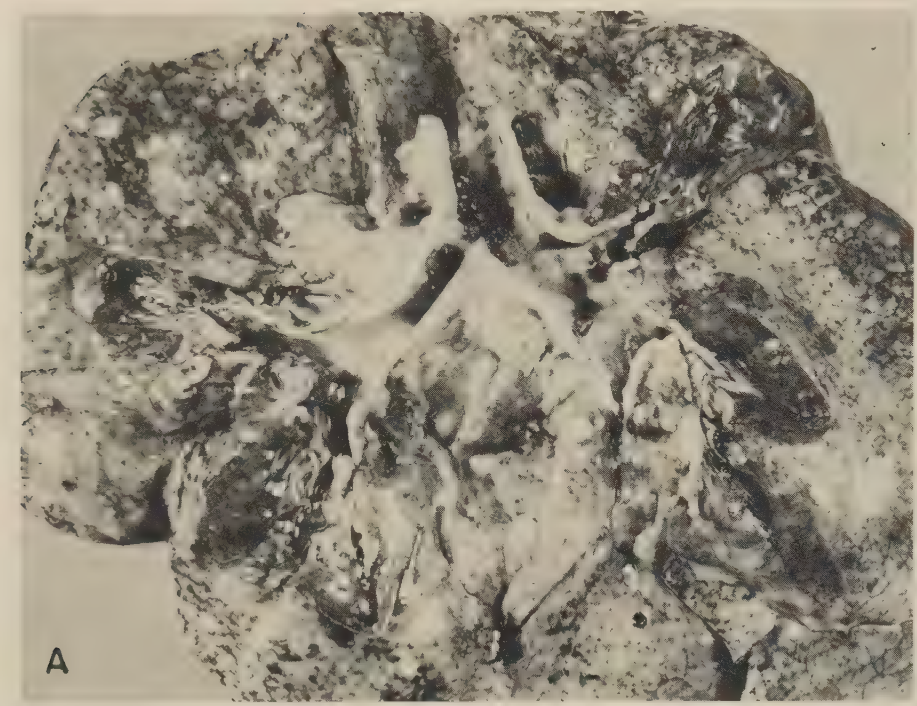
Acute hemorrhagic tracheitis, in young man dying of typhus fever. Massive mucosal hemorrhage; edema; inflammatory cell infiltration of tunica propria and epithelium. Gland duct distended with mucus. x80.



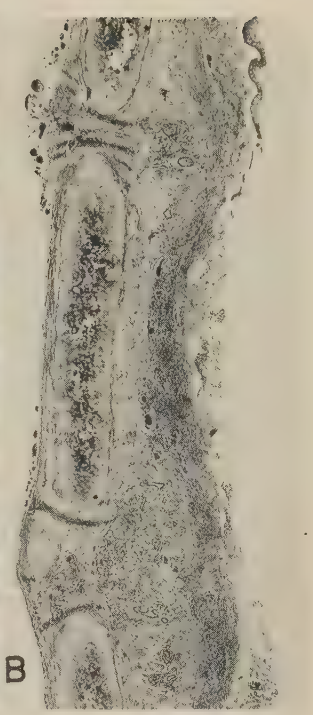
Acute necrotizing tracheobronchitis, in man who died of peritonitis, pulmonary abscesses and bronchopneumonia. Ragged ulcerated surface coated with dense layer of inflammatory exudate, erythrocytes and fibrin. Congested thrombosed vessels. Atrophic glands; periglandular exudate. x50.



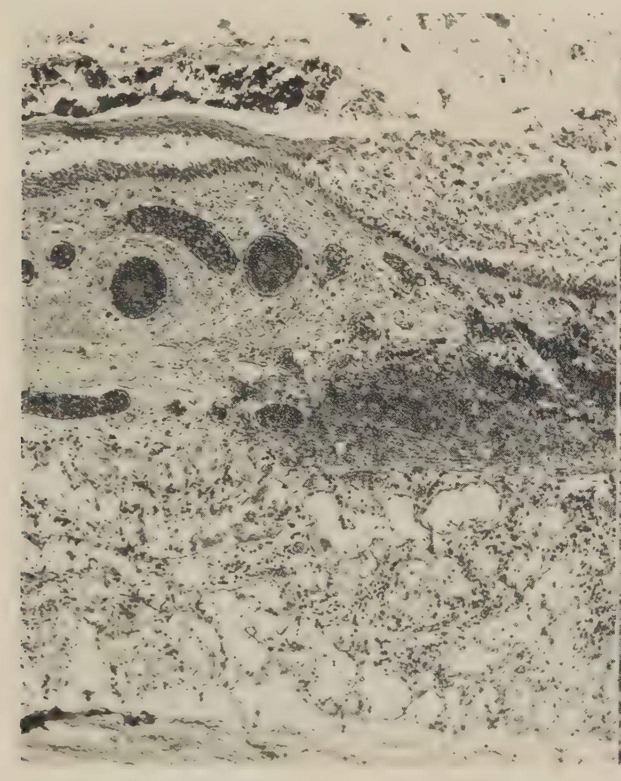
Acute tracheitis due to poisoning by accidental ingestion of approximately 125 Gm. of ferrous sulfate (given with barium sulfate). Chocolate color; dyspnea; melena; death shortly thereafter. Congestion and thrombosis of vessels. Erosion of epithelium. x80.



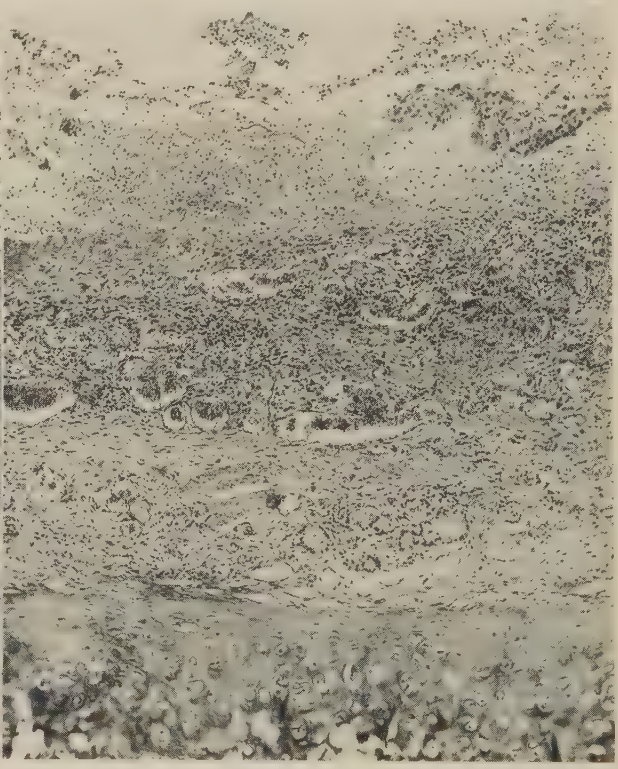
Edema and hyperemia of tracheobronchial tree. It contains remnants of castlike accumulations of partially charred, dark brown, adherent exudate, resembling a pseudomembrane. When pulled away, irregular mucosal erosions were found. Patient trapped in burning building; larynx illustrated in previous plate.



Ulcerative tracheitis in man who lived twelve days following severe burns. x13.

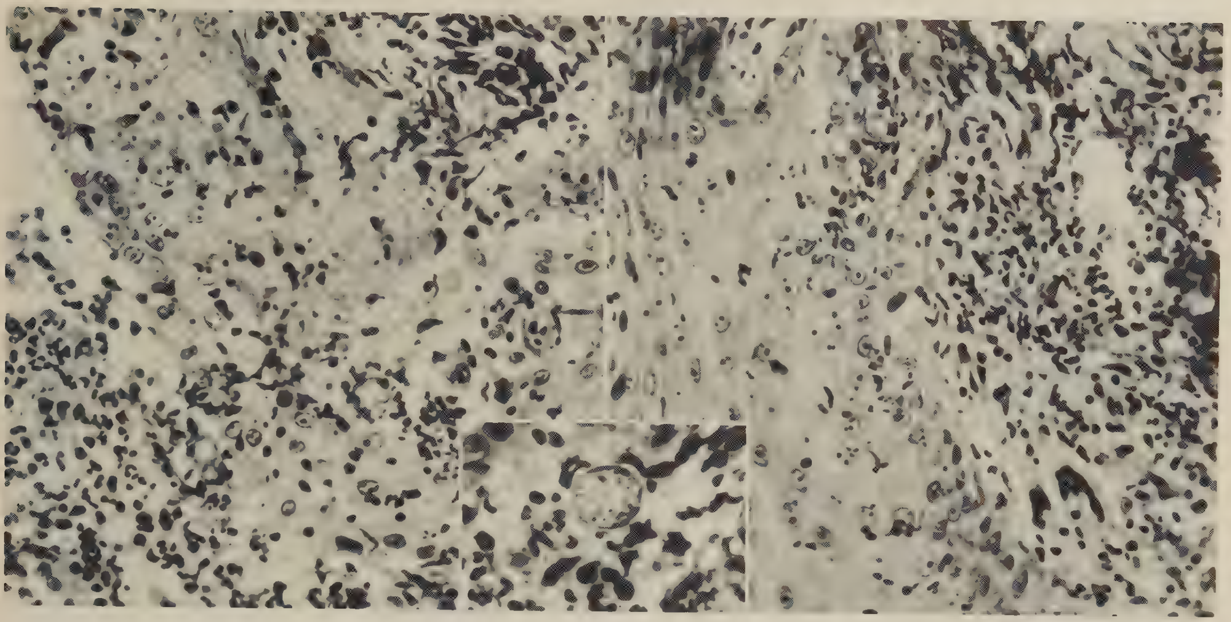


Section of trachea from **A.** Black granular material in surface exudate; intraepithelial vesication; pronounced mucosal edema; vascular congestion, and interstitial hemorrhage. x83.

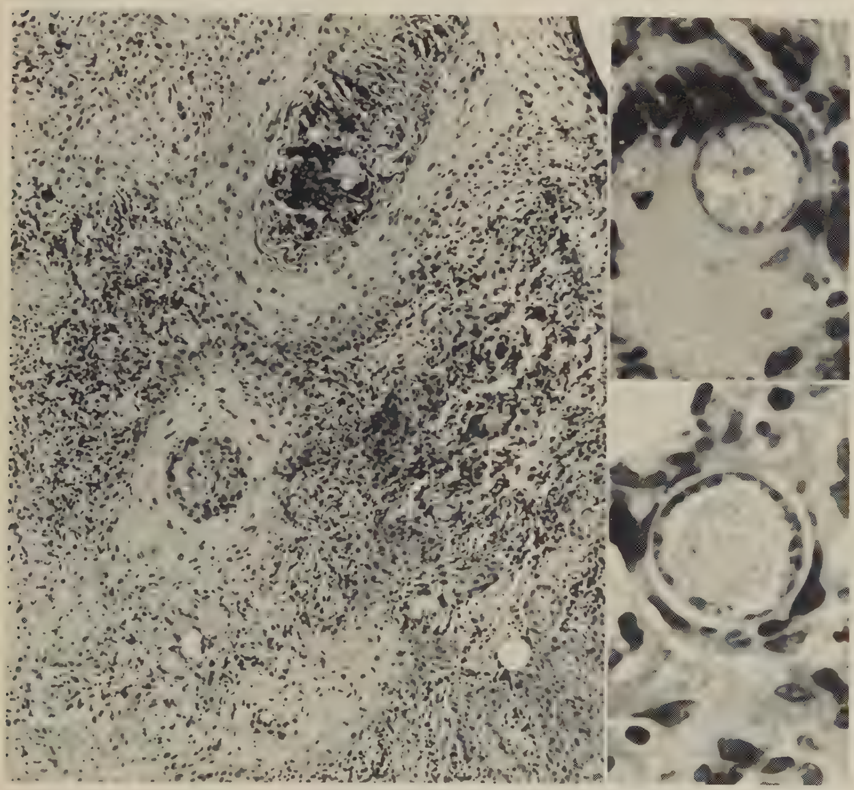


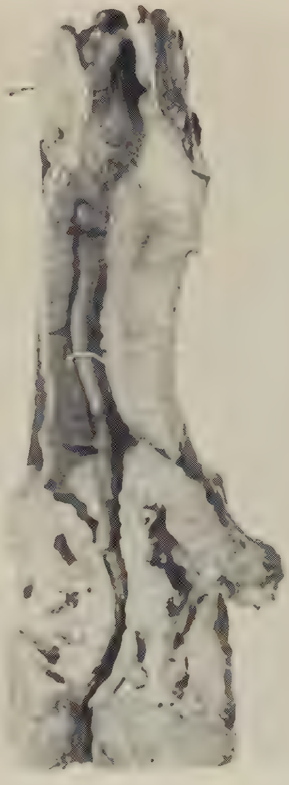
Section of trachea from **B.** Extensive ulceration of superficial mucosa; pronounced vascular congestion; dense inflammatory and hemorrhagic exudate in lamina propria. x62.

COCCIDIOIDOMYCOSIS, TRACHEA
ASCARIS LUMBRICOIDES IN TRACHEA



Coccidioidomycosis, initially diagnosed from this tracheal biopsy. Fields from two tiny biopsy fragments containing several spherules. One of these is shown in *inset*. x750. The inflammatory reaction is both suppurative and granulomatous. Giant cells are present in *right* field. This degree of reactive epithelial metaplasia and hyperplasia is rare in the trachea. Both x275.



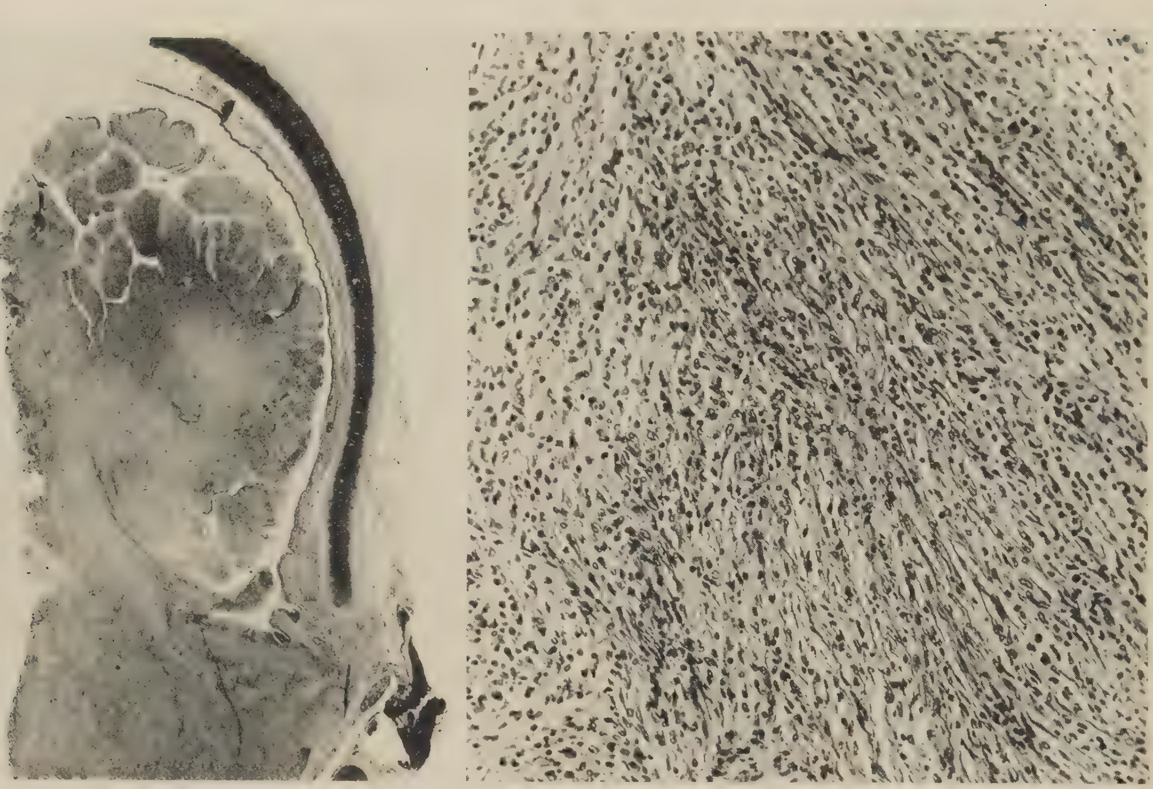


Coccidioidomycosis, skin of face *(left)*. Subsequent lesion in same patient. Pseudoepitheliomatous hyperplasia; intense suppurative and granulomatous inflammation. Two maturing spherules *(center)*, upper one within large giant cell. x120, x700, x700.

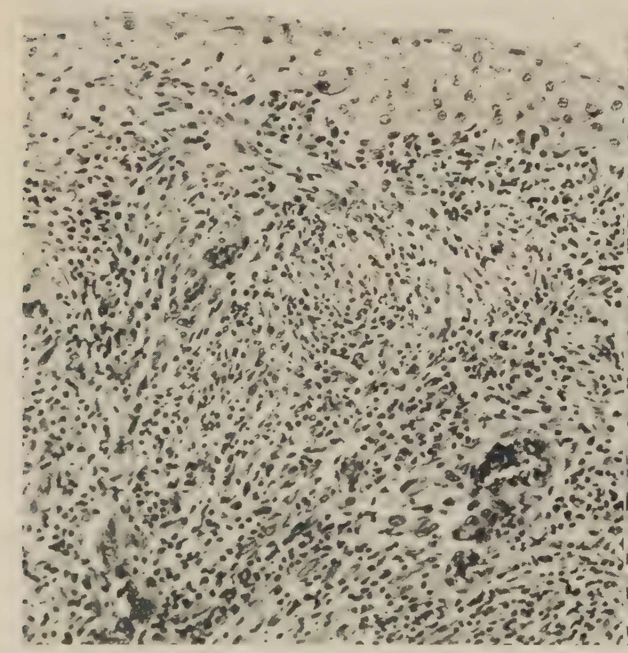
Ascaris lumbricoides *(right)*. Adult nematode as found at autopsy in trachea and right bronchus of 17 year old private who "suddenly choked and died in five minutes." In heavy infections the adult worm may be vomited, or may migrate from small intestine to stomach and esophagus and then pass into larynx and trachea.

INFLAMMATORY PSEUDOTUMOR, TRACHEA

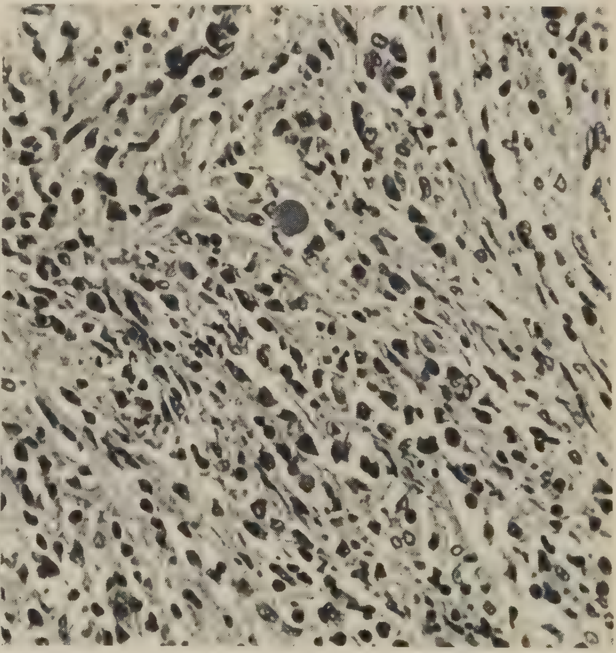
(INFLAMMATORY FIBROID POLYP)



Inflammatory polypoid tumor almost completely occludes tracheal lumen. Cause of death in young man with "asthma" for several years, but no bronchoscopic examination. x5. Representative field from center of tumor. All parts of cellular fibrous stroma diffusely, often heavily, infiltrated by inflammatory cells, predominantly plasma cells. x165.

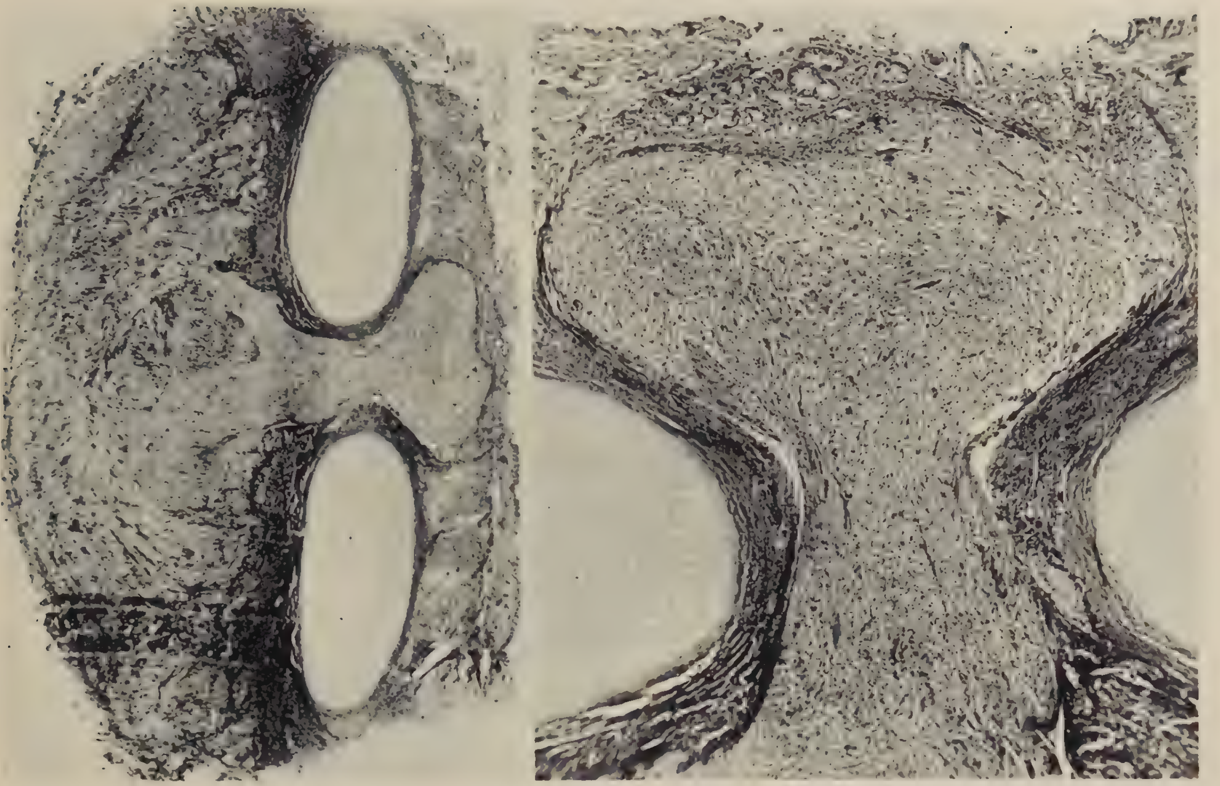


Surface of polyp. Squamous metaplasia of epithelium; numerous inflammatory cells; fibrous tissue, occasionally whorled or in wavy strands about blood vessels. x165.

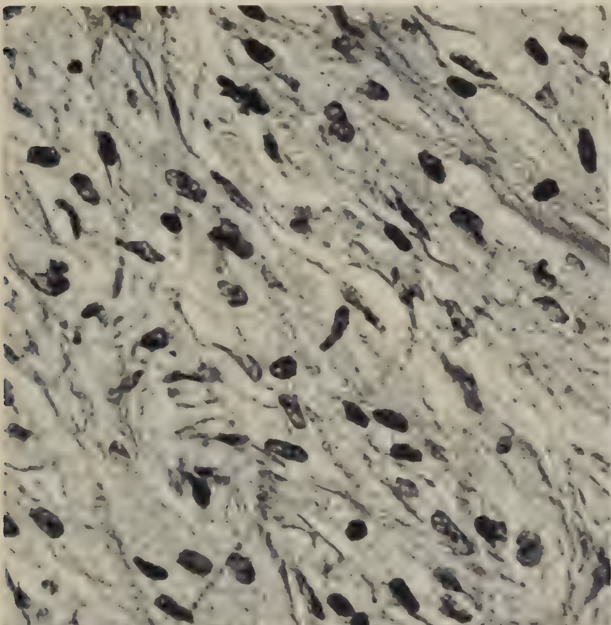


Base of polyp. Collagenous tissue heavily infiltrated by plasma cells, some mononuclear cells, and lymphocytes. Round Russell body slightly above center. x355.

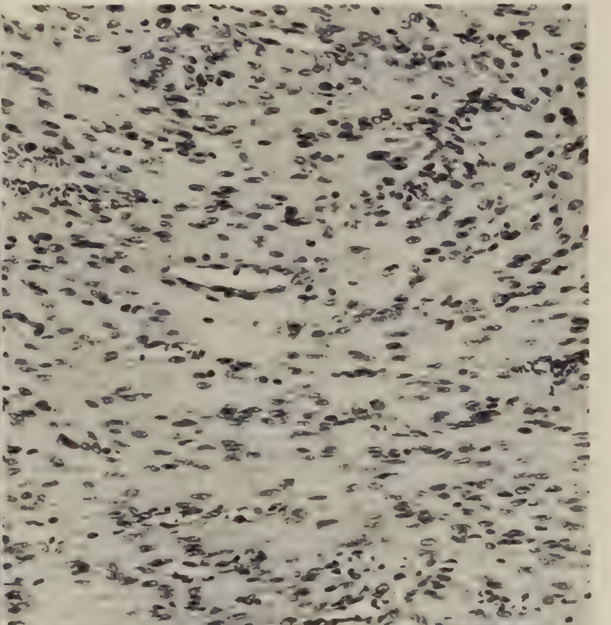
Cytologic and structural pattern of this lesion resembles the "inflammatory fibroid polyp" of the stomach, recently described by E. Helwig.



Neurofibroma, portions of which resemble granular cell myoblastoma. An incidental finding at autopsy in a 20 year old Negro soldier. Dumbbell-shaped tumor, largely extratracheal, extends between two cartilaginous rings to tracheal mucosa. No striated muscle within or around the mass. x13, x48.



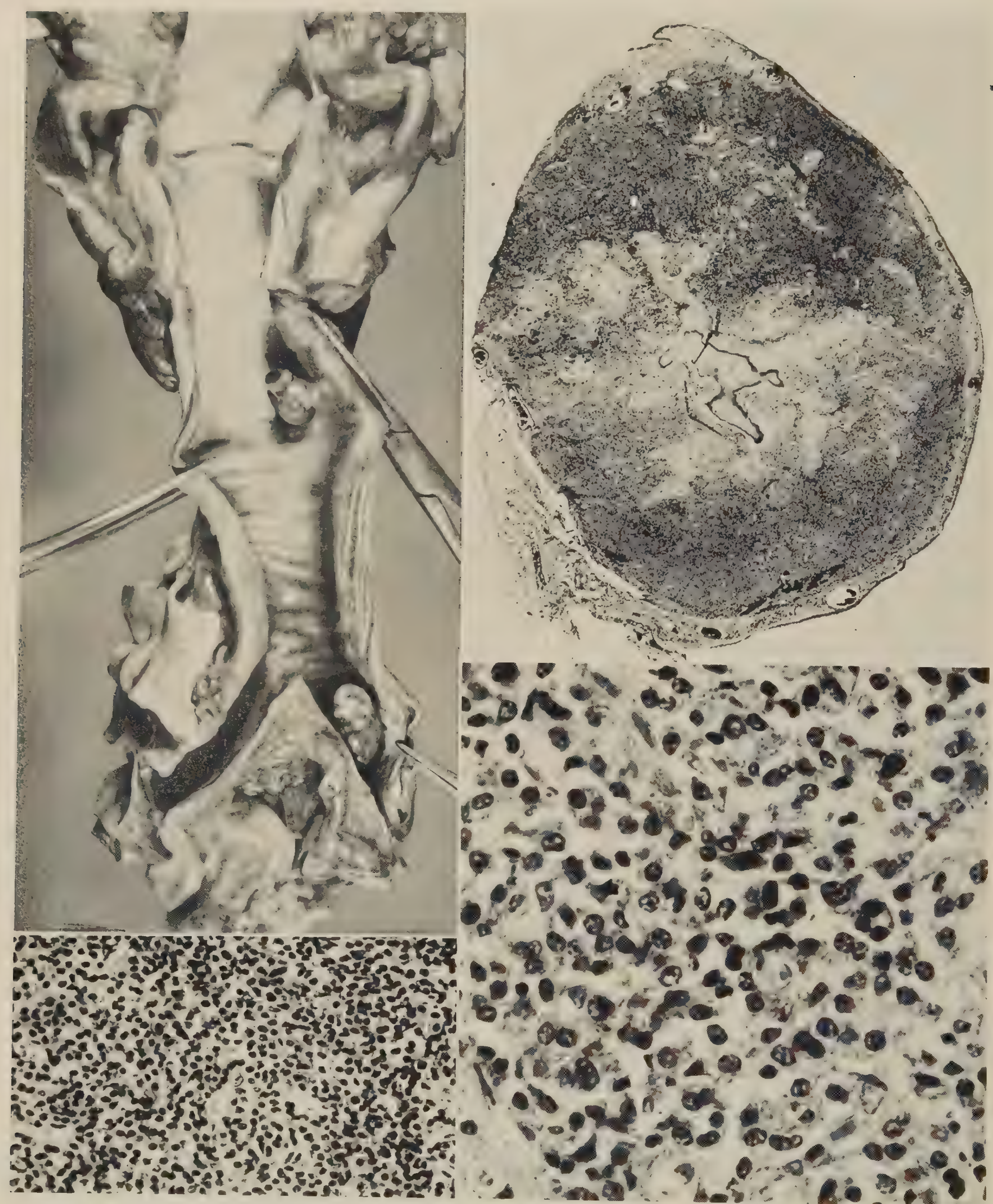
Field of same fibrillar tumor at higher magnification. Within mass of proliferating cells and fibers, granular eosinophilic cytoplasm suggestive of granular cell myoblastoma. x515. Nerve fibers demonstrated within mass.



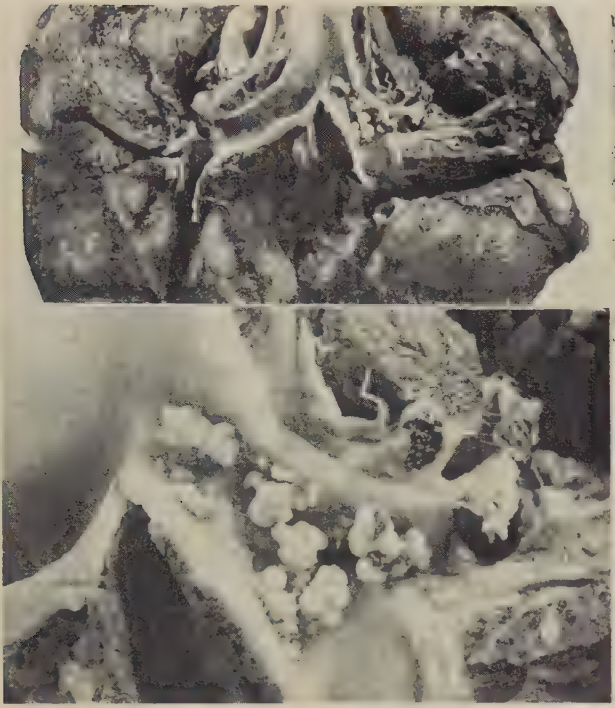
Inflammatory pseudotumor of the trachea at the coryna of a young man. Neurofibroma was initial diagnosis because of densely fibrous areas with orientation and alignment of fibroblasts suggestive of palisading. x165.

PLASMACYTOMA, TRACHEA

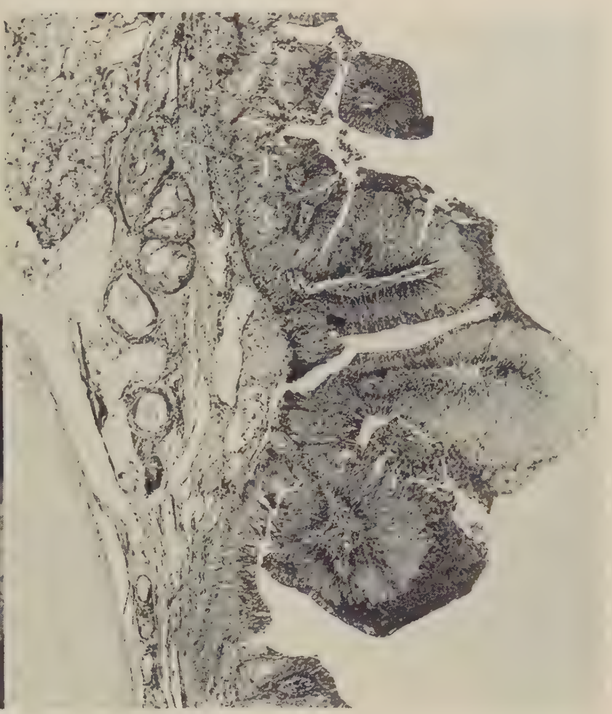
(PLASMA CELL TUMOR)



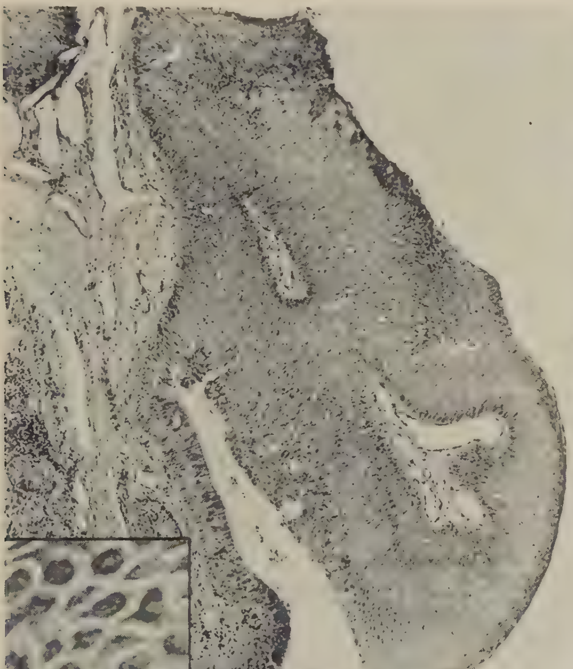
Multiple plasma cell tumors of the upper respiratory tract. 44 year old man, hoarse for five years, occasional dyspnea and dysphagia. The large tumors of the trachea and right main bronchus are easily seen; smaller tumors of vocal cords and epiglottis are indistinct; nodules in nasopharynx and oropharynx also found at autopsy. *Upper right:* **polypoid tracheal tumor.** The amyloid-like protein deposits also resemble the protein casts in kidneys in multiple myeloma. x13. *Lower:* differentiated uniform cells resembling plasma cells. Binucleate, trinucleate, and occasionally atypical cells. x300, x600. Unique tumor—no plasmacytoma of the trachea has been cited in comprehensive reviews. (W.L. Mattick, Buffalo, N.Y.)



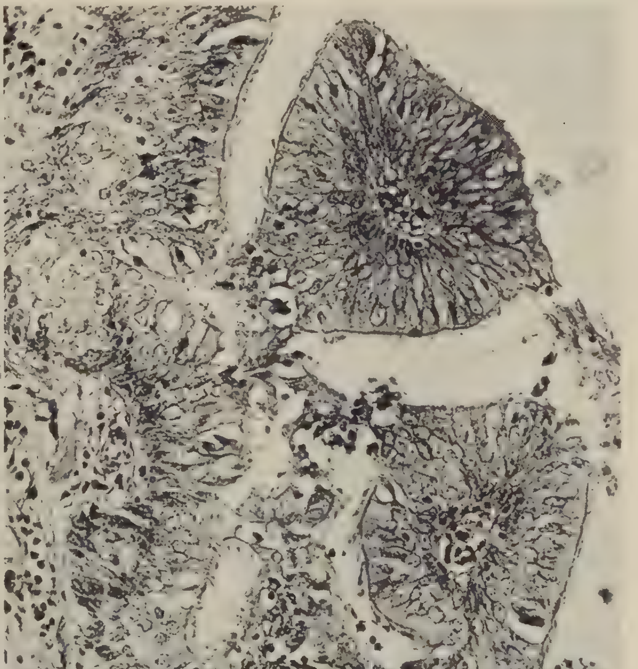
Papillomas of trachea and right bronchus. Autopsy finding in 53 year old man with wheezing and dyspnea, hospitalized few days previously for tuberculosis. Many friable papillomas were lost before photography. (I. Stergus, Rome, Ga.)



Structural features of a papilloma from trachea. Finger-like stromal projections are covered by hyperplastic squamous epithelium. Note squamous metaplasia of epithelium in ducts of glands. x62.



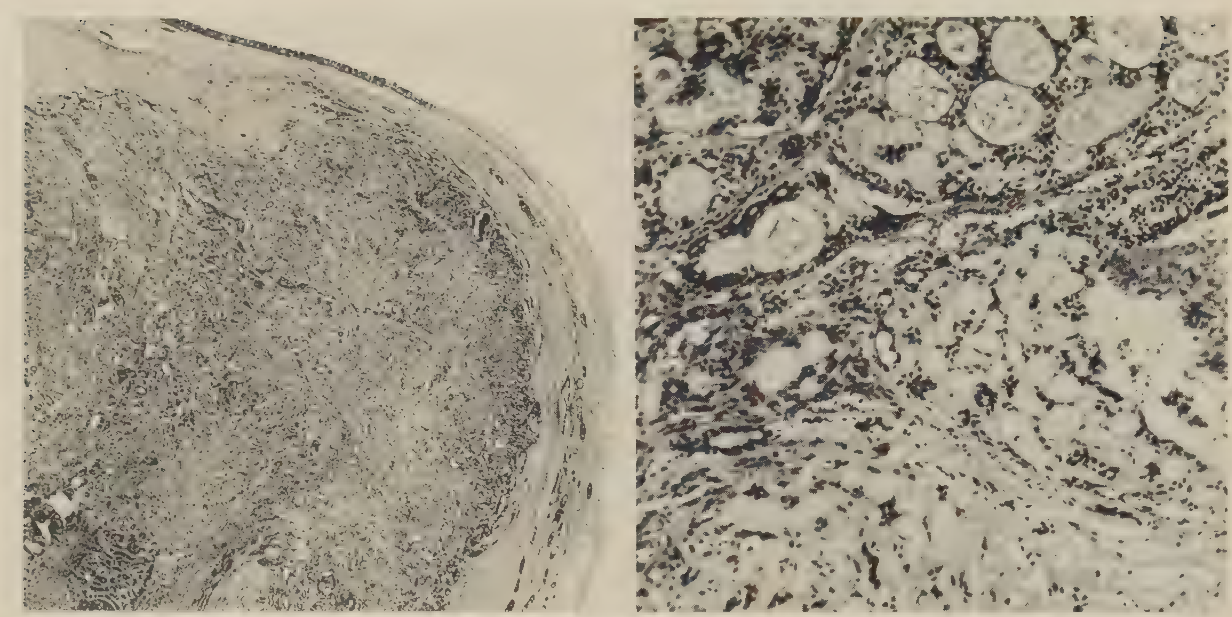
Acanthosis and squamous metaplasia in this early papilloma. Proliferative activity of basal layer; squamous differentiation with intercellular prickles at its tip *(inset)*. x75.



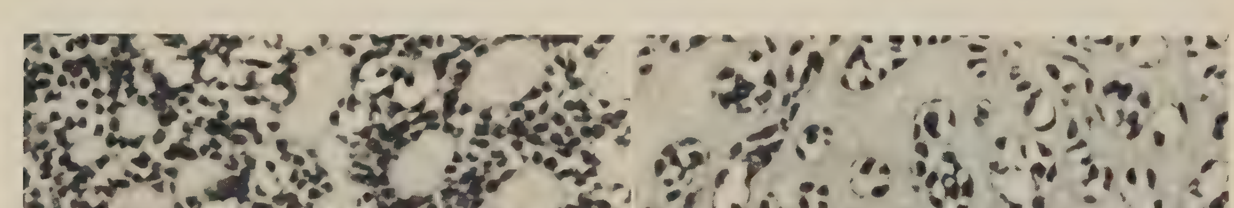
Modified, but still ciliated respiratory epithelium in an early papilloma from same case. Contains occasional mucicarmine-positive goblet cells and focal true stratification of cylindrical cells. x235.

ADENOID CYSTIC CARCINOMA, TRACHEA

(CYLINDROMA; TRACHEAL "ADENOMA")

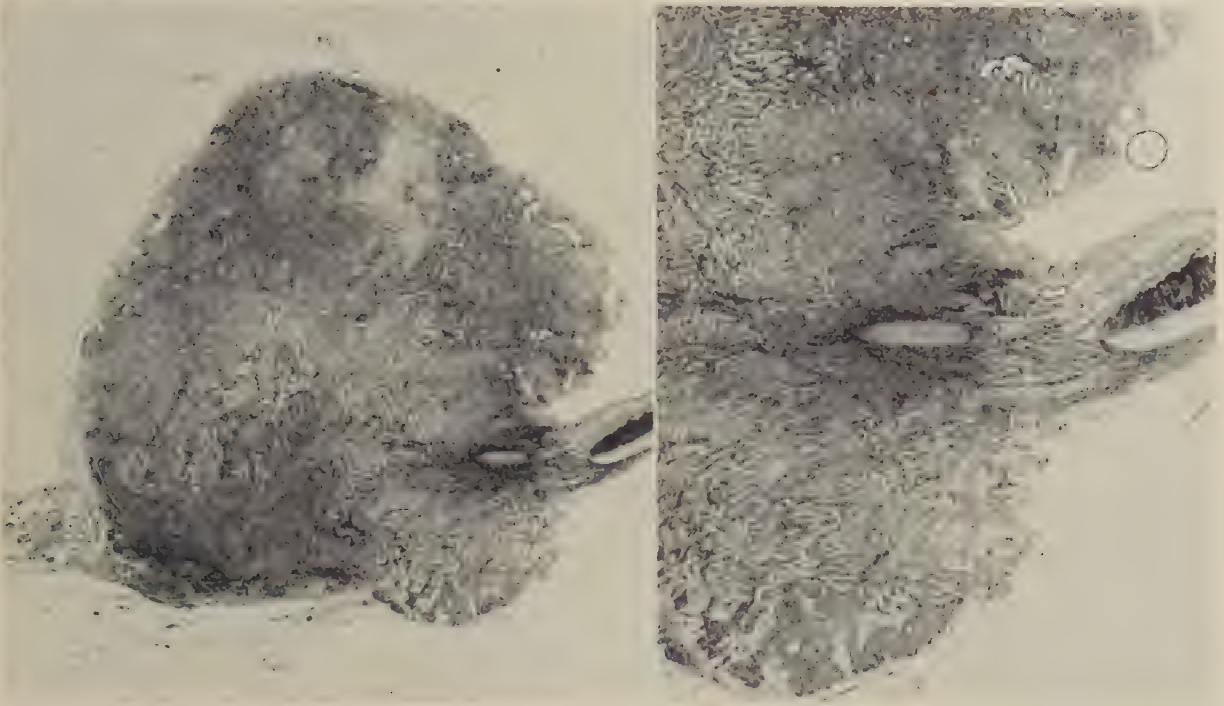


Large polypoid tracheal mass with wide base, incompletely removed bronchoscopically. Adult man with hemoptysis for two years, dyspnea for one month. Recurrence two years later, with occasional hemoptysis, cough and dyspnea. A mass bulging through the right side of the trachea, ¾ inch long, was completely resected with 7 tracheal rings. x21. *Right:* mucicarminophilic adenoid cystic and hyalinized "cylindromatous" patterns in the same field. x125. Apparently well two years later.

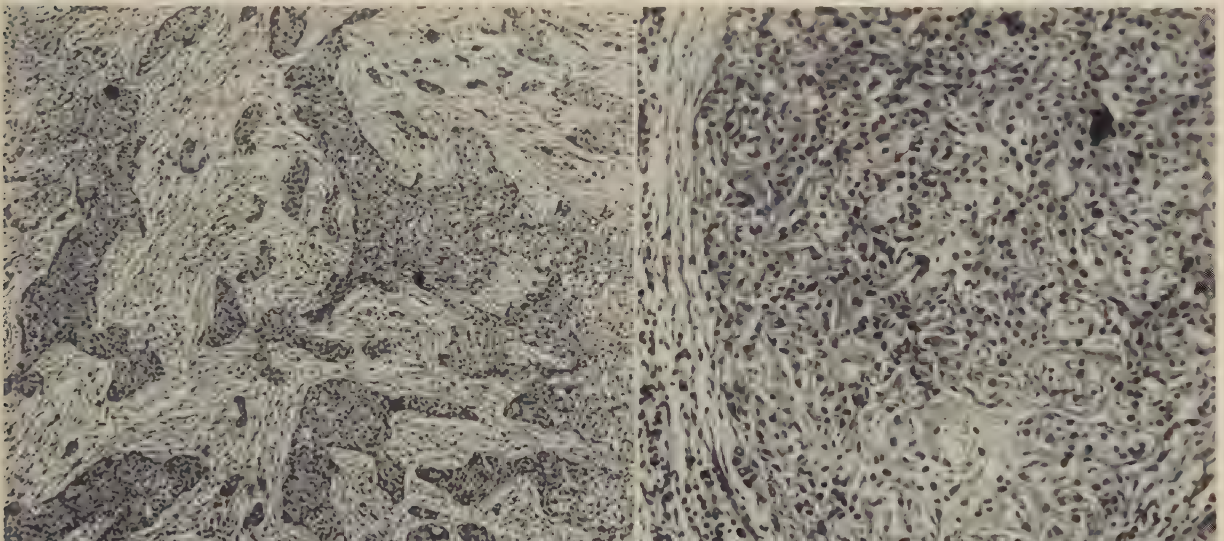


Phases in transition from adenoid cystic to hyalinized structure. Fields from same tumor. **A** and **B.** The foamy secretion within and also around cellular groupings was strongly mucicarminophilic. **C.** Condensing intercellular material was moderately positive; and in **D,** pale pink in mucicarmine stains. All x300. (M.J. Schlesinger and B. Castleman, Boston, Mass.)

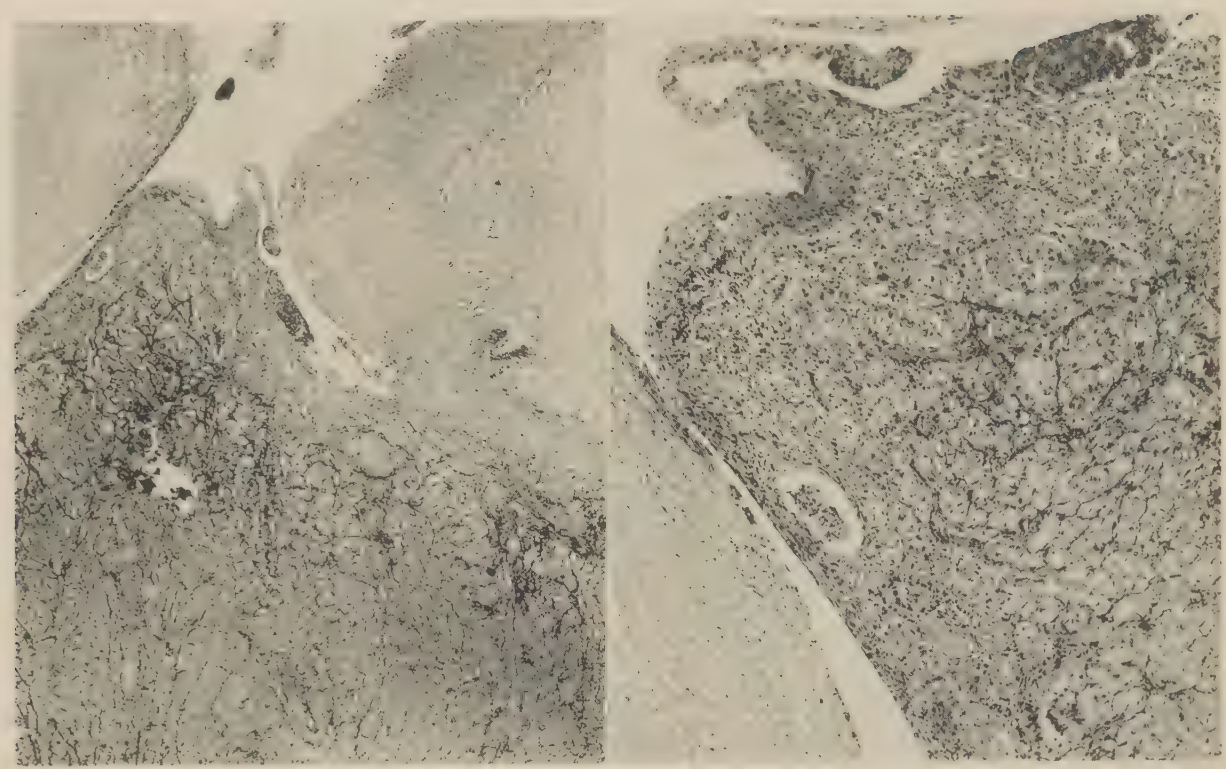
TRACHEAL “ADENOMA”
(ADENOCARCINOMA; MUCOEPIDERMOID CARCINOMA?)



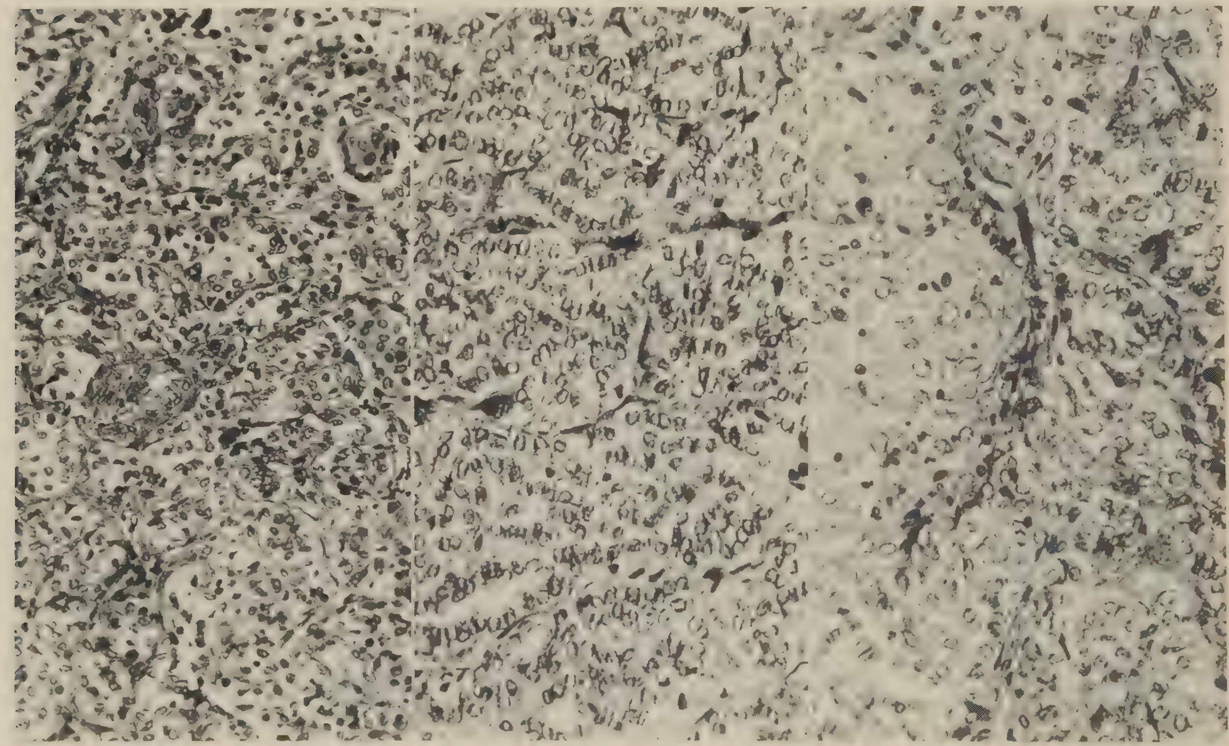
Rare type of so-called tracheal adenoma in a 70 year old woman with wheezing and dyspnea for two years. *Left:* polypoid mass projecting into lumen (at top) has destroyed and extended through tracheal cartilage and, at lower right, through the outer elastic fibrous membrane. x6. *Right:* magnified area. Tracheal mucosa, glands and cartilage at top right. Infiltrating nests and strands of tumor. x12.



Representative structural pattern at base and center of tumor, distant from surface and mucosal glands. Cells of probable “intermediate” type with well defined epidermoid differentiation in many areas (not shown). x62. *Right:* cellular nests such as these contained strongly mucicarmine-positive cells, clusters of cells, and secretion. x125. Probably analogous to mucoepidermoid carcinoma.

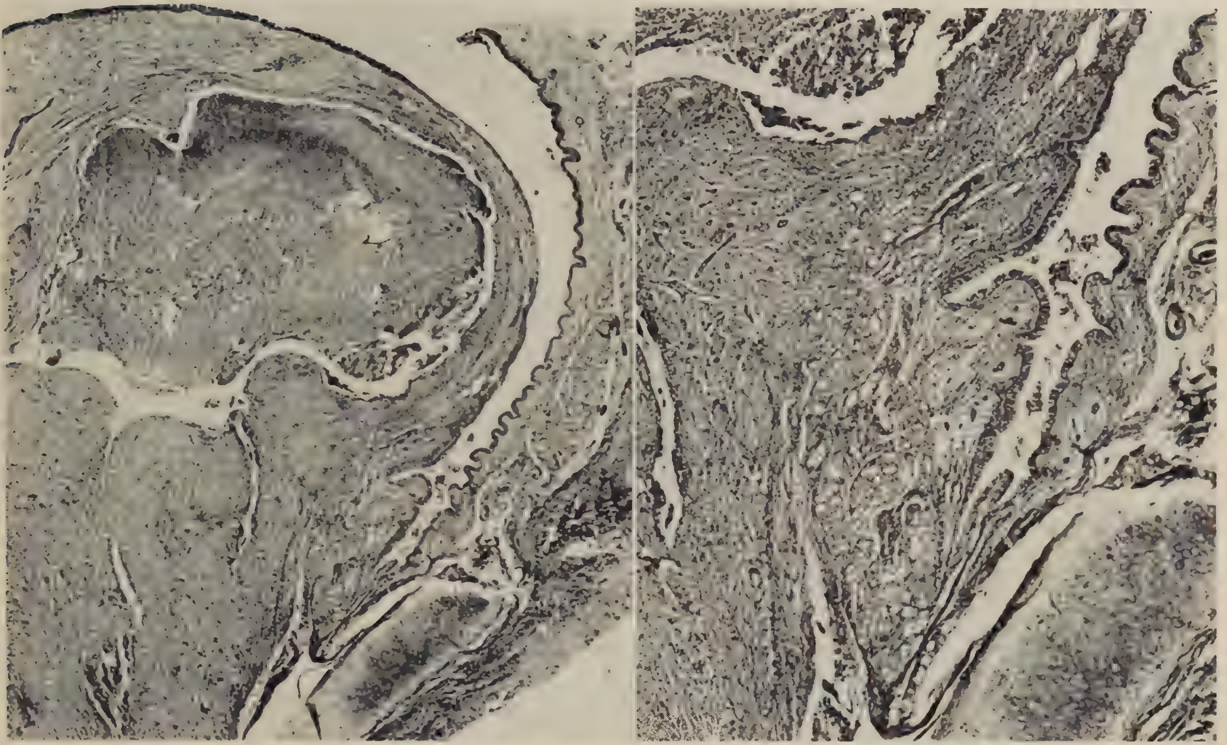


Tumor diagnosed as tracheal "adenoma" in a 61 year old woman with dyspnea and expiratory wheeze. Repeated recurrences causing obstruction finally necessitated tracheotomy. Irradiation therapy unsuccessful. Death with metastasis five years after first biopsy. Extension of tumor to the mucosal surface of the trachea. x31, x76. (L. Schwartz, N.Y., N.Y.)

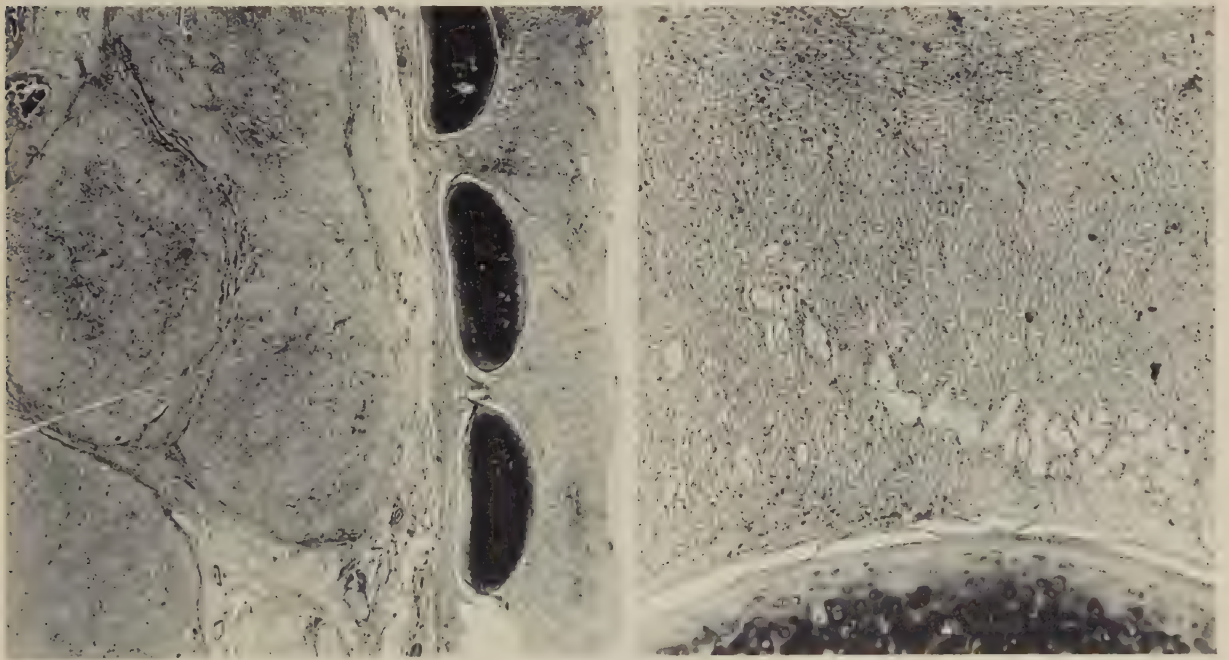


Originally considered primary in the trachea, the cell type and acinar arrangement are not inconsistent with thyroid origin. x185, x275, x275. The tumor arose from the anterior wall of the trachea in the region of the thyroid, but neither absence nor presence of a thyroid tumor was recorded.

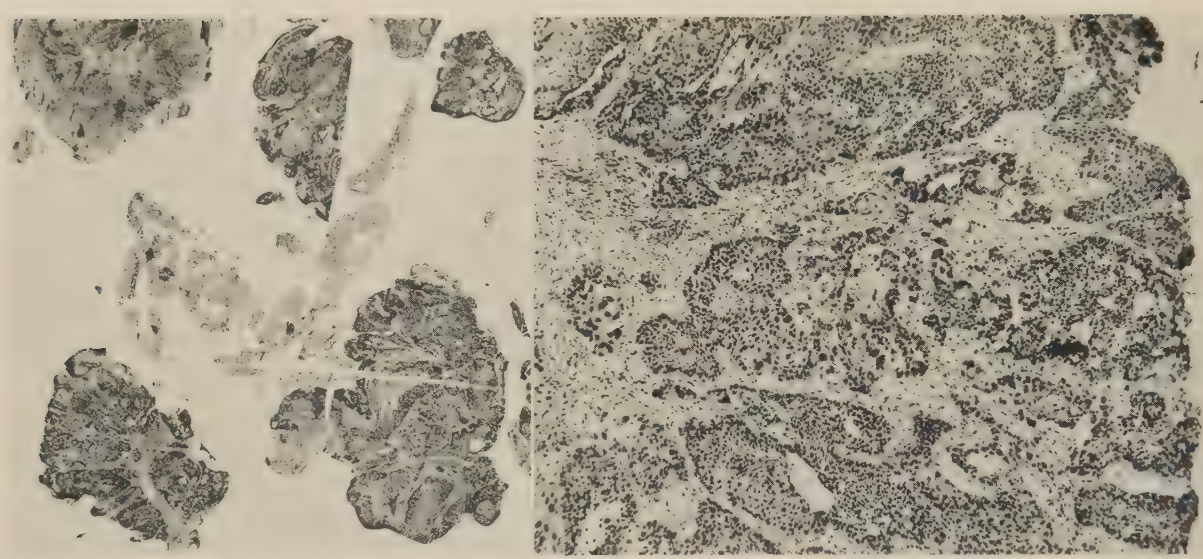
ADENOCARCINOMA, TRACHEA
MALIGNANT LYMPHOMA (HODGKIN'S DISEASE)



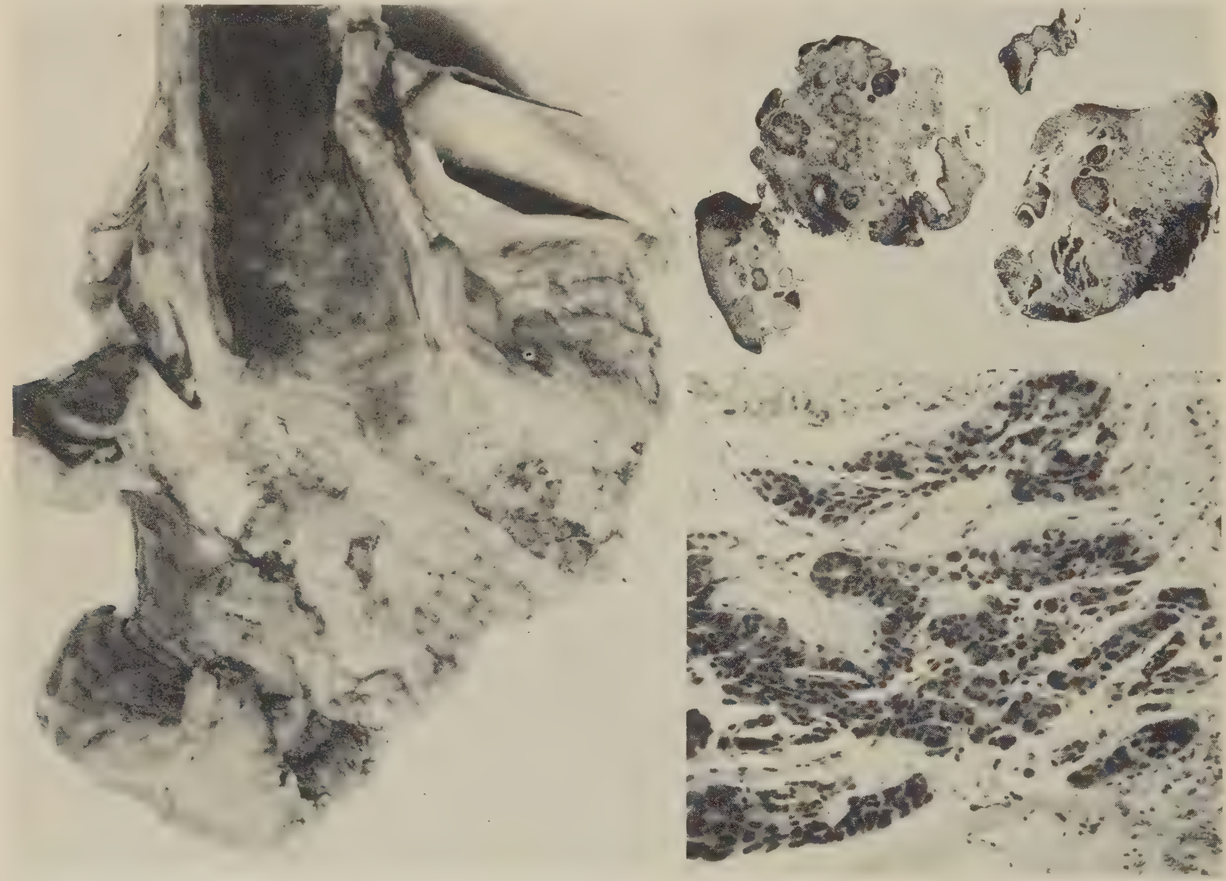
Adenocarcinoma, possibly primary in trachea. Large polypoid tumor within tracheal lumen had cytologic and structural features compatible with origin in tracheal glands or secondary extension into trachea from a "large cervical mass." x10, x24. Accurate decision regarding primary site is impossible because of lack of material and poorly performed autopsy with inadequate description of tracheal tumor, cervical mass and other metastases.



Hodgkin's disease, trachea. *Left:* longitudinal section through three cartilaginous rings. Massive involvement of paratracheal nodes at left. Greatly thickened tracheal mucosa at right. x8. *Right:* full thickness of diffusely involved mucosa with polymorphous cellular infiltrate, typical of Hodgkin's. Widely separated and atrophic glands at bottom. The numerous Reed-Sternberg cells in this field can be distinguished as the larger black dots. x48.



Epidermoid carcinoma, primary in trachea. Bronchoscopic specimen *(left)* from a lobulated mass on anterior tracheal wall 2 cm. above the bifurcation, in a 52 year old man with uncontrollable cough for one year. x10. *Right:* surface of well differentiated tumor. Keratinizing foci in other areas. x55. Repeated endoscopic resection and electrocoagulation were required to keep airway clear until death seven years later, with only cervical metastases.

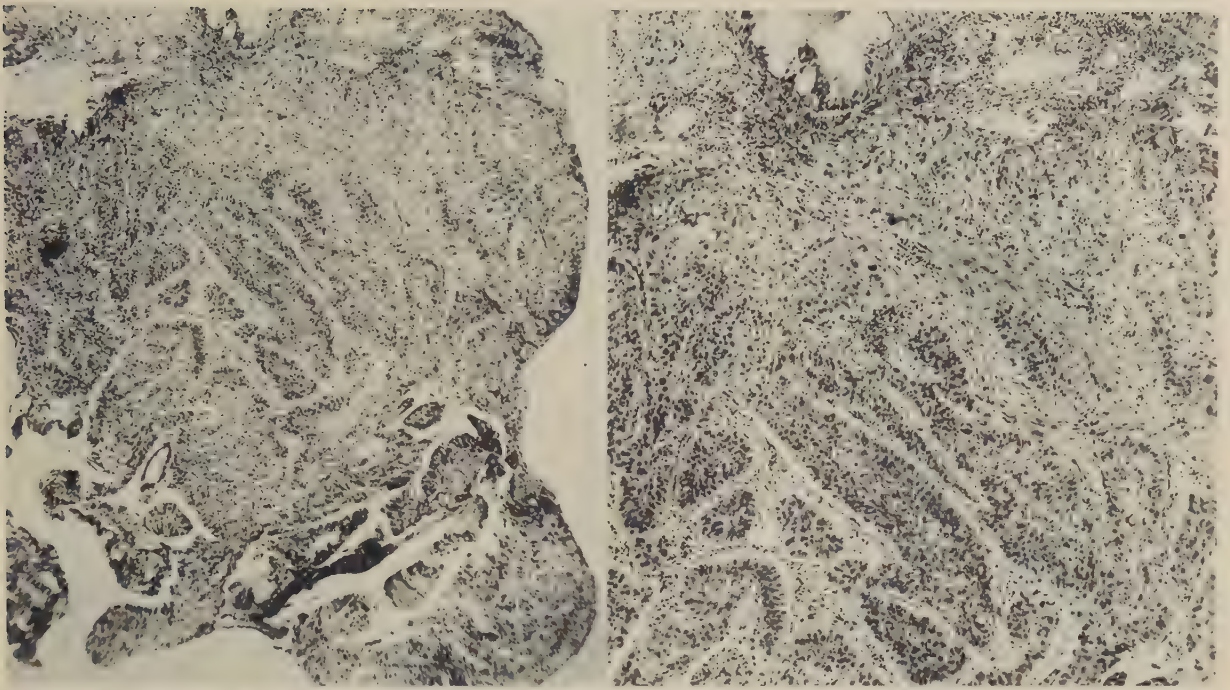


Infiltrating carcinoma in autopsy specimen has broadened and eroded coryna, extended anteriorly, superiorly, and inferiorly into both bronchi. (P. Holinger and E. Hirsch, Chicago.) *Right:* last bronchoscopic biopsy of tracheal tumor (x13) contained nests of cells apparently within endothelium-lined spaces. x115.

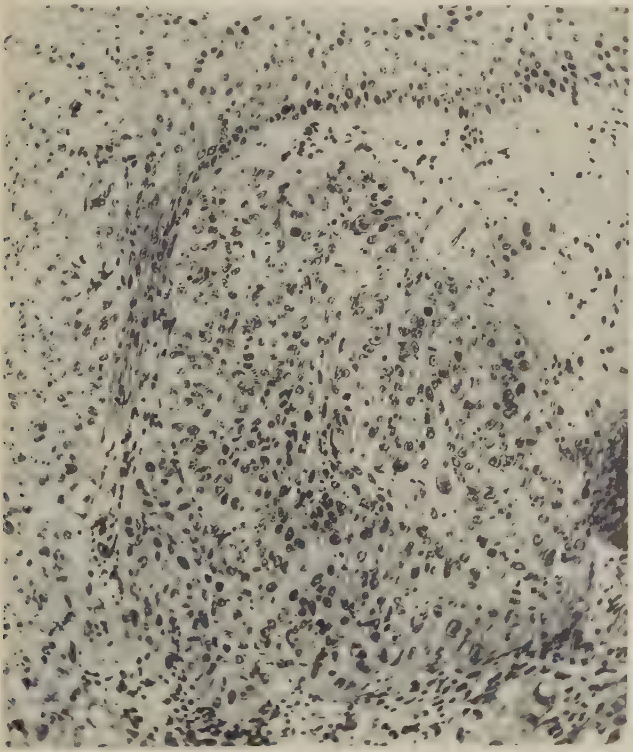
Tracheal biopsy specimens must be diagnosed cautiously, since primary epidermoid carcinoma of the trachea is very rare. Far more frequent is secondary extension into the trachea from primary carcinoma of adjacent organs, particularly the bronchi.

SECONDARY CARCINOMA, TRACHEA

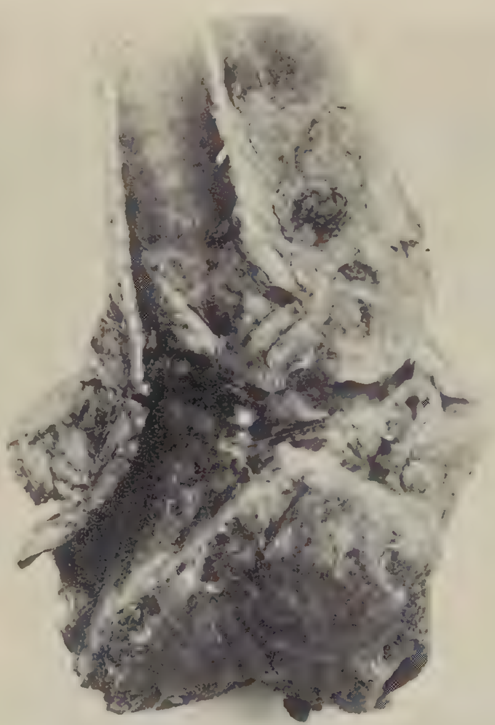
EXTENSION FROM BRONCHOGENIC CARCINOMA



Bronchoscopic specimen diagnosed primary carcinoma of the trachea. *Left:* the representative, adequate biopsy specimen has been well preserved, and is a technically excellent section for microscopic diagnosis. x48. *Right:* tracheal mucosa infiltrated by carcinoma. Normal respiratory epithelium above. x62.



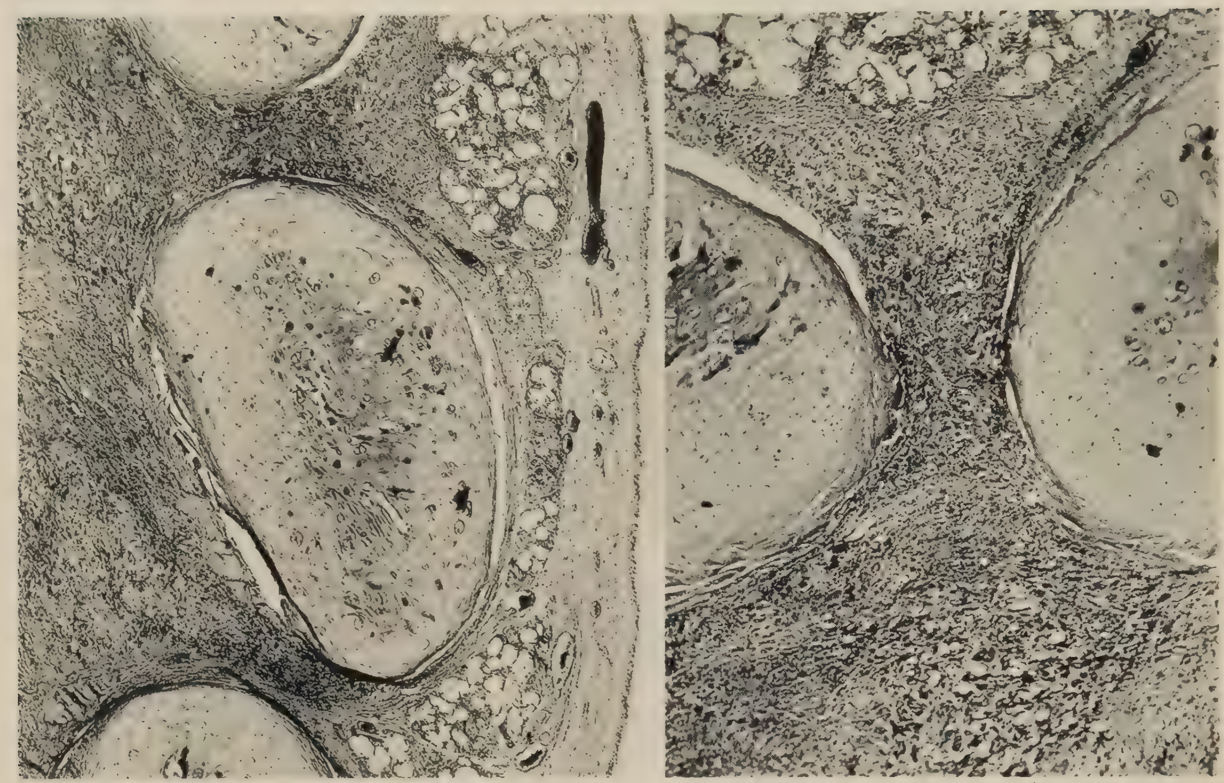
Primary bronchogenic carcinoma with direct extension to trachea was found in subsequent studies of the same patient. The carcinoma has extended to the surface epithelium of the trachea in this field. x160.



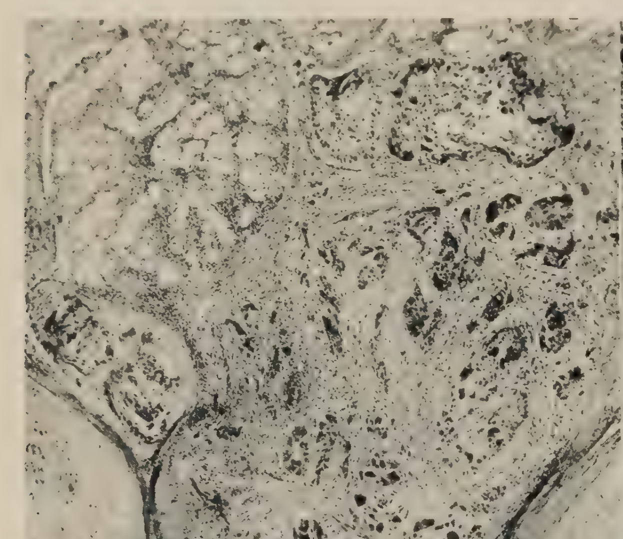
Direct extension from metastatic bronchogenic carcinoma in tracheal, parabronchial and mediastinal lymph nodes has resulted in raised nodular masses of tumor projecting into the lumen of trachea and bronchi. (P. Holinger and E. Hirsch, Chicago.)

SECONDARY CARCINOMA, TRACHEA

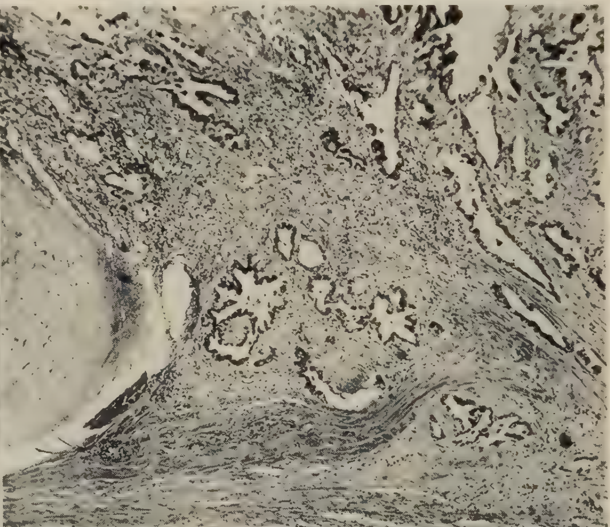
EXTENSION FROM LYMPH NODE METASTASES



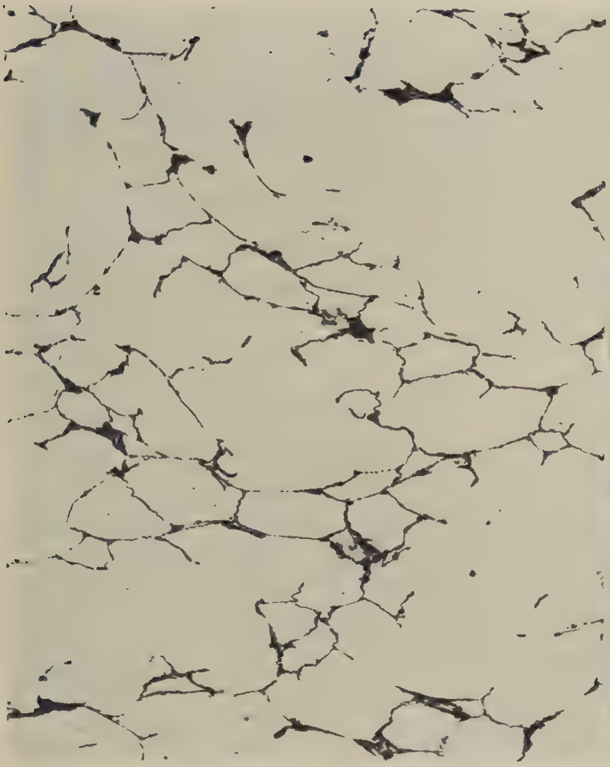
Metastatic bronchogenic carcinoma, undifferentiated, in lymph nodes has extended to paratracheal soft tissues and is invading trachea between cartilaginous rings. The tough elastic fibrous membrane has been destroyed by the undifferentiated tumor. x31, x48.



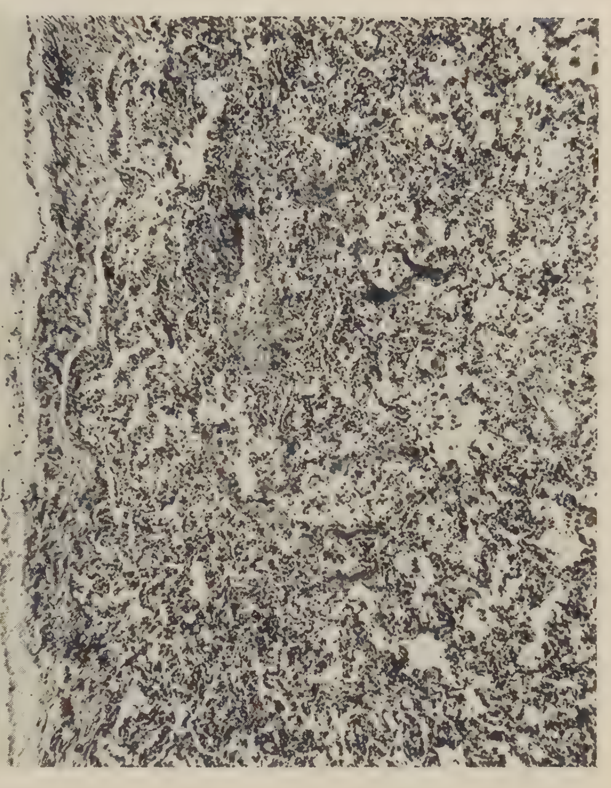
Metastatic bronchogenic carcinoma, pleomorphic epidermoid, has extended from tracheal lymph nodes, between tracheal rings to the mucosa. x48.



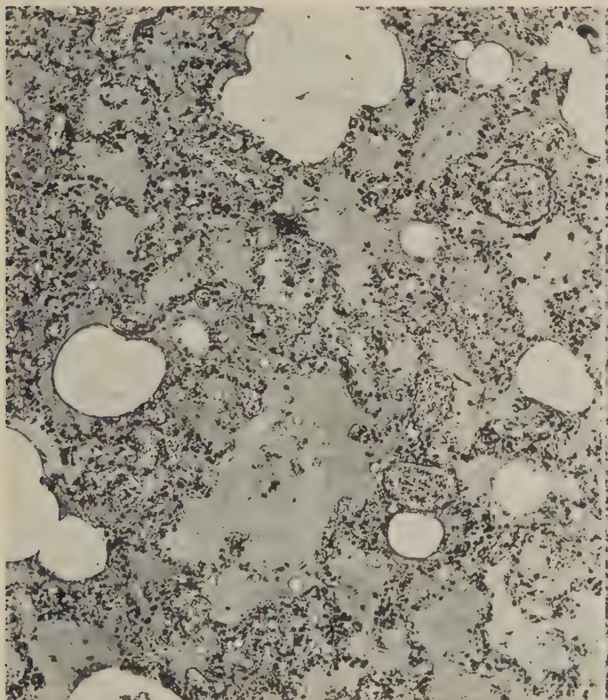
Metastatic adenocarcinoma, well differentiated, in paratracheal lymph nodes, from a primary tumor of the pancreas, is invading tracheal mucosa. x48.



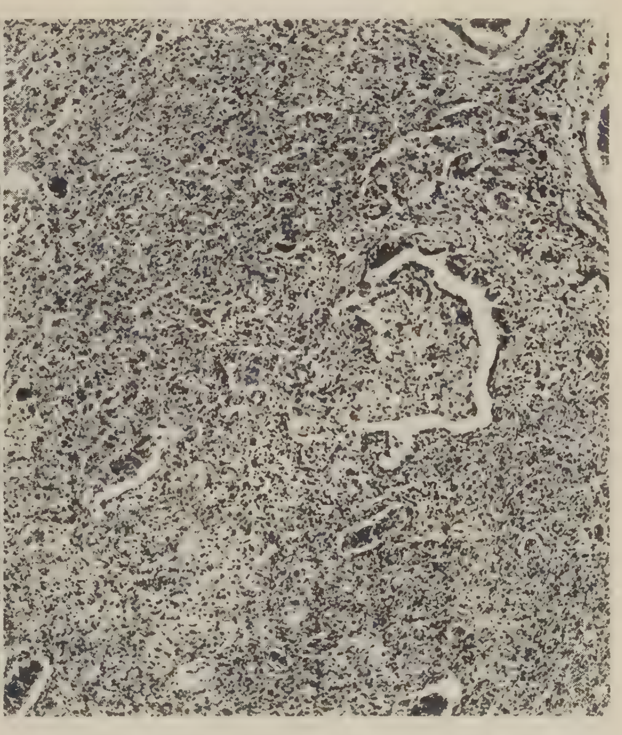
Emphysema, characterized by overdistension of air spaces, marked thinning and loss of elasticity of alveolar walls and rupture of latter to form the very large spaces. x48.



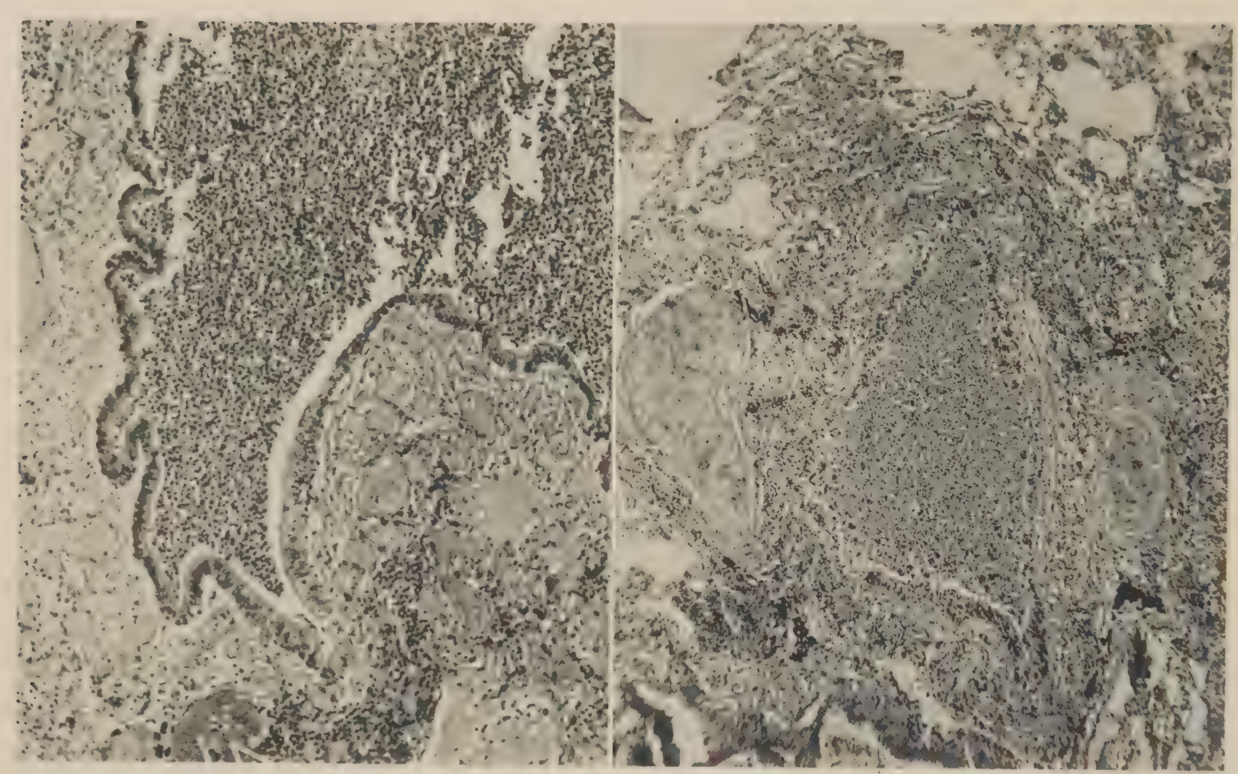
Atelectasis, the collapse of all or any portion of a lung, may be attributable to compression of the lung, as in this case, or to bronchial obstruction. x60.



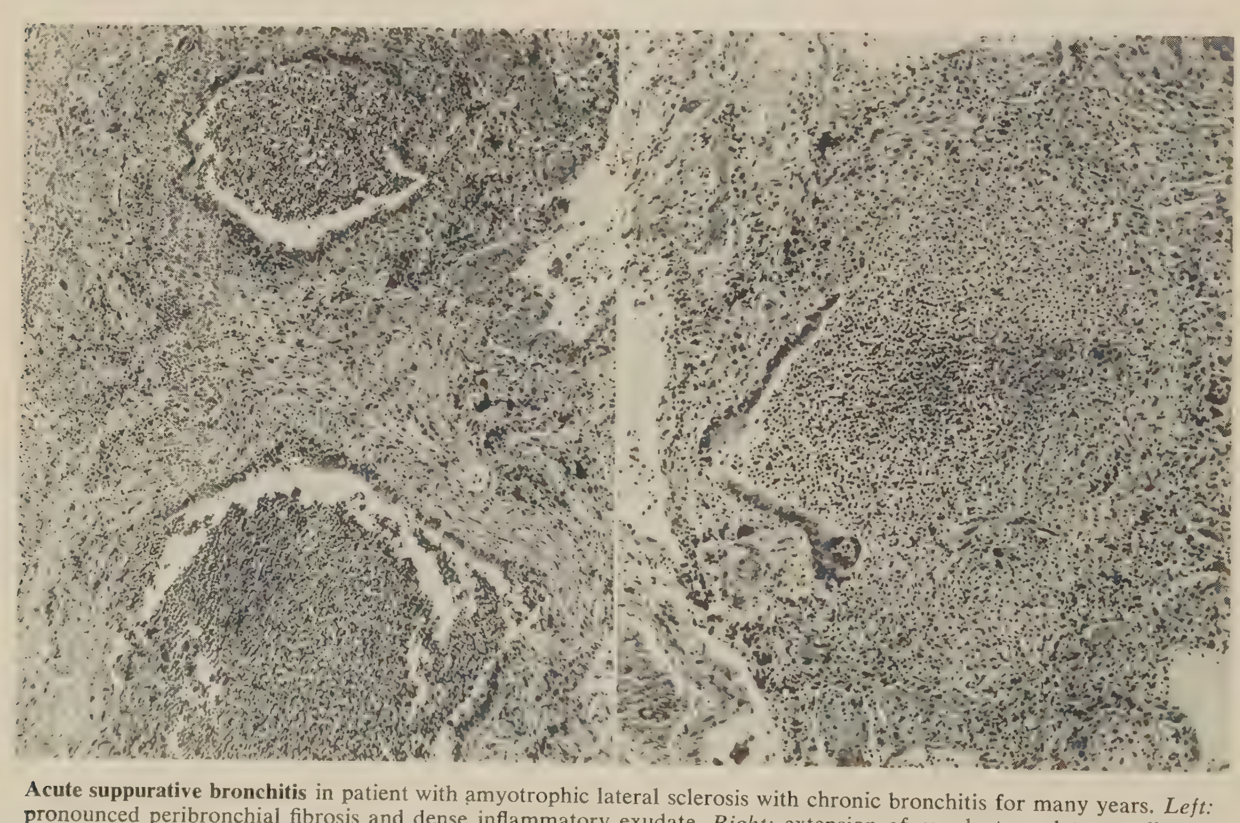
Edema. Air spaces are filled with extravasated fluid containing sufficient protein to coagulate during fixation. The fluid may have resulted from inflammation or circulatory failure (transudate). x70.



Congestion and hemorrhage, acute, intrapulmonary. Vessels engorged and air spaces filled wih blood. Mucosa of included bronchus is eroded. From patient dying twelve days after thermal injury. x70.

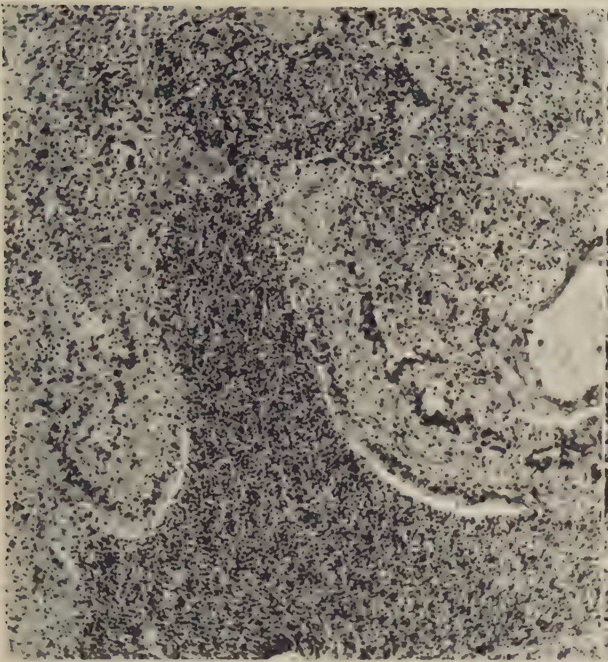


Terminal purulent bronchitis in patient with laryngectomy for carcinoma. Purulent exudate fills bronchi. *Left:* marked vascular congestion. *Right:* desquamation of epithelium and focal ulceration of bronchus. Inflammatory exudate in peribronchial tissues. x200, x145.

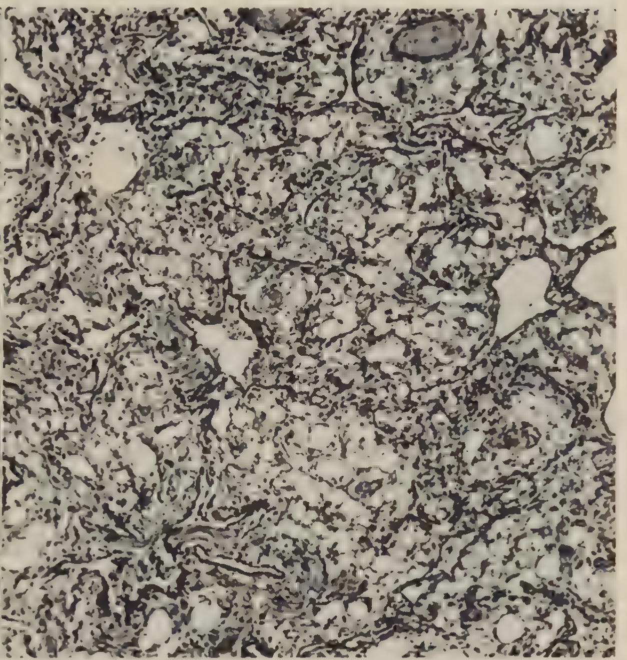


Acute suppurative bronchitis in patient with amyotrophic lateral sclerosis with chronic bronchitis for many years. *Left:* pronounced peribronchial fibrosis and dense inflammatory exudate. *Right:* extension of purulent exudate to adjacent pulmonary parenchyma from large ulceration of bronchial mucosa. Both x145.

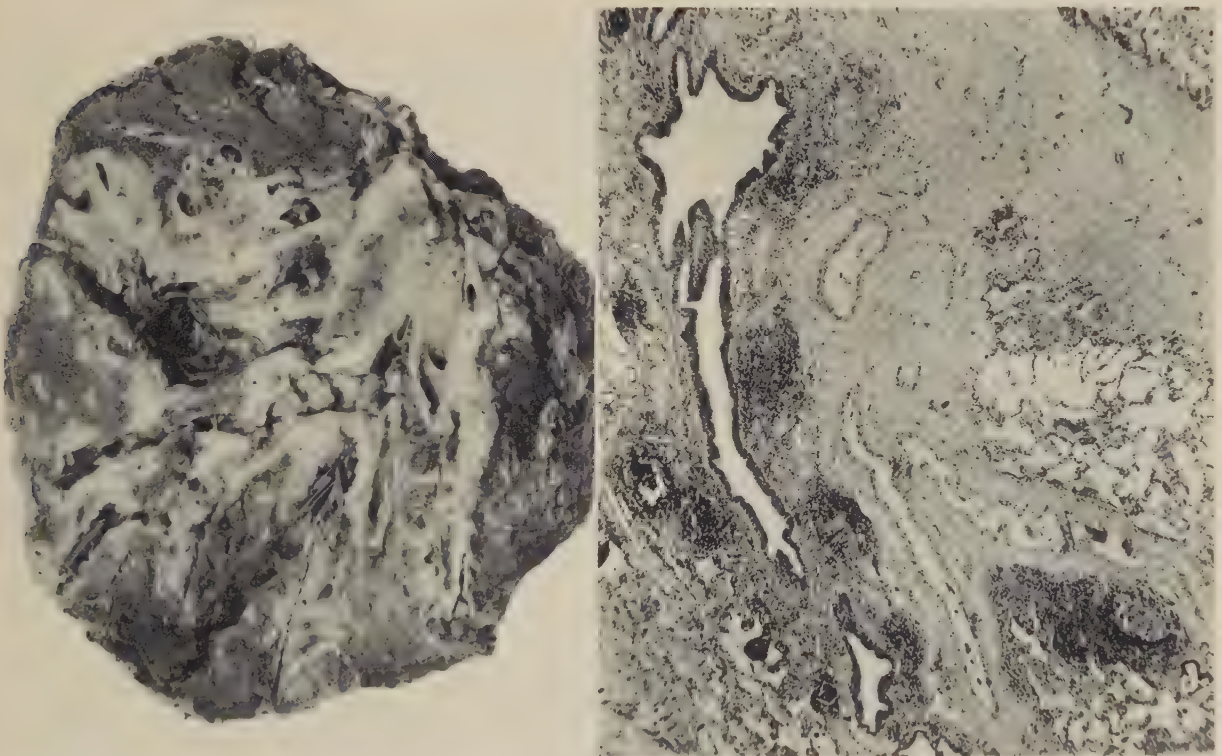
ASPIRATED FOREIGN BODY WITH BRONCHIECTASIS



Aspiration pneumonia in patient with recurrent carcinoma of the upper respiratory tract. Purulent exudate fills bronchus, has eroded epithelium, and extended through large focal ulcerations to peribronchial tissues and adjacent alveoli. x90.

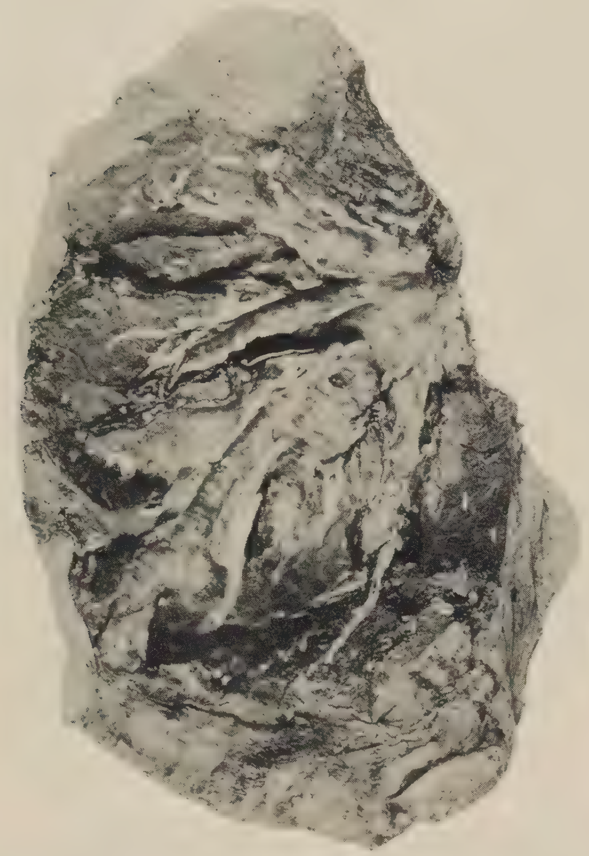


Lipid pneumonia. Air spaces in consolidated foci filled with vacuolated macrophages containing phagocytosed oil. x90. Aspirated animal oils such as cod liver oil and vegetable oil are the most frequently implicated agents.

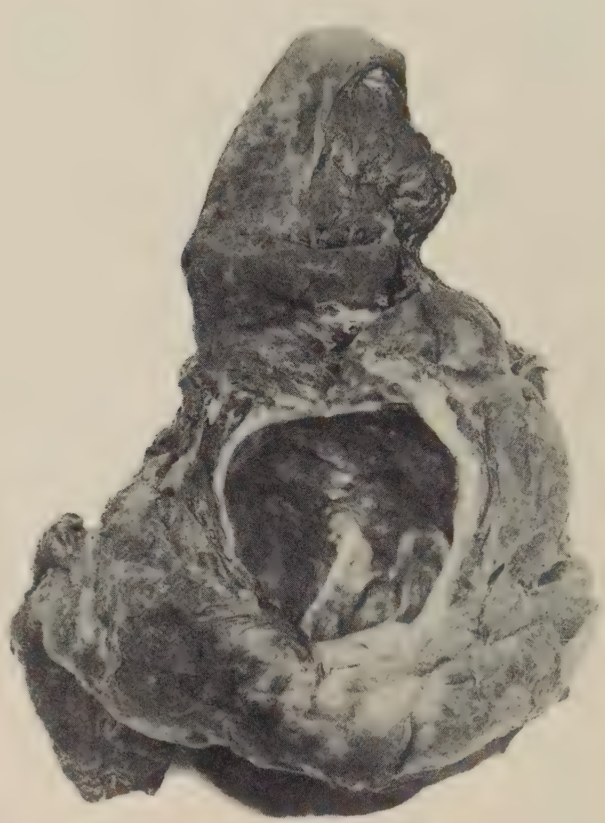


Bronchiectasis resulting from aspirated pine needles still present in dilated bronchi. Areas of suppuration, extensive peribronchial fibrosis, and focal atelectasis. *Right:* dilated bronchus with no evident cartilage or smooth muscle fibers; dense fibrous tissue; chronic inflammatory exudate. Note formation of lymphatic nodules. x48.

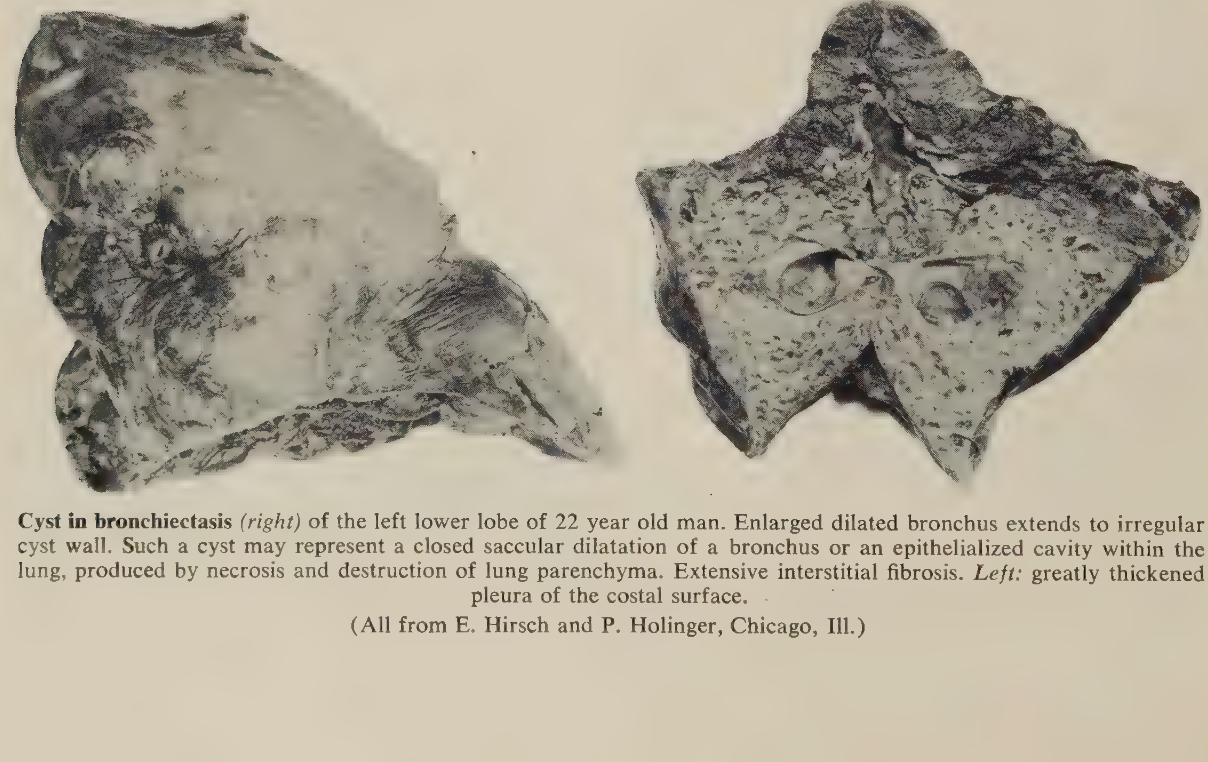
BRONCHIECTATIC CYSTS



Chronic bronchiectasis of the right lower lobe in a 30 year old man. "Cylindrical" dilatation of greatly enlarged bronchi. Fibrosis and atelectasis of adjacent lung tissue; thickened pleura. (Specimen has been bisected and anterior part turned upward.)

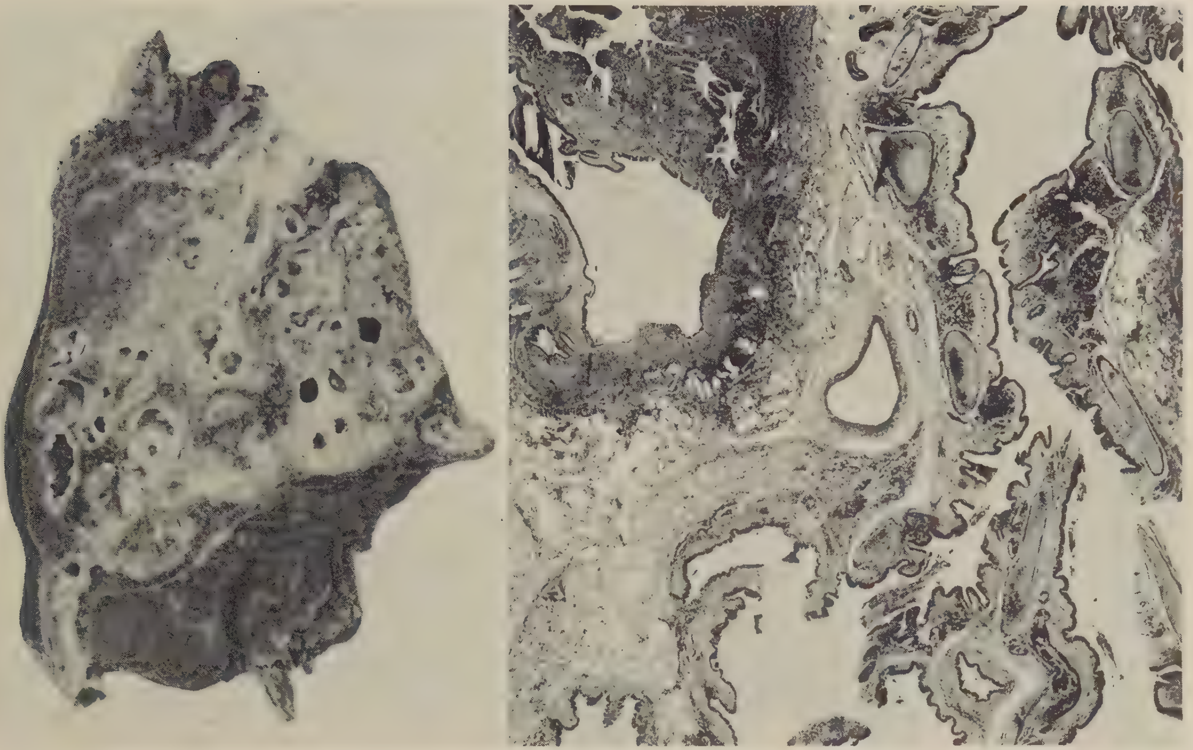


Solitary cyst (congenital?) in a 12 year old girl with chronic bronchiectasis and fibrosis of the right lower lobe. It is difficult to determine whether congenital anomaly or developmental factors play a role in the pathogenesis of such lesions.

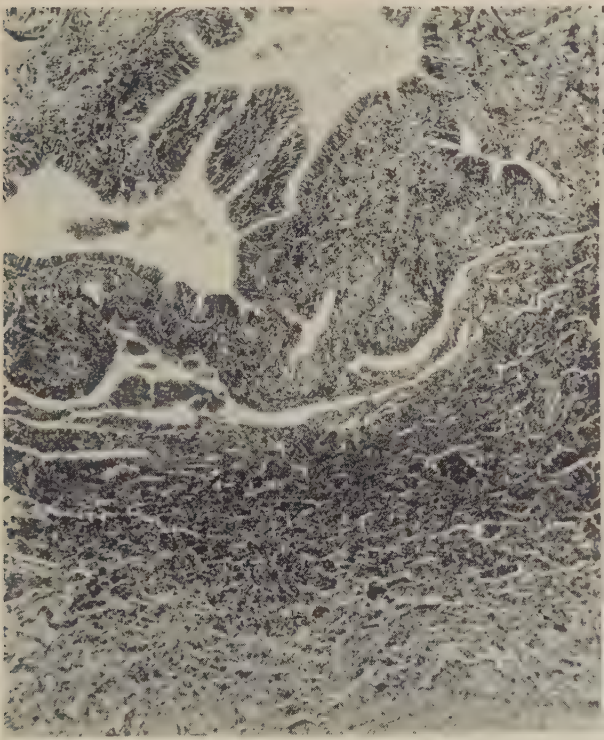


Cyst in bronchiectasis *(right)* of the left lower lobe of 22 year old man. Enlarged dilated bronchus extends to irregular cyst wall. Such a cyst may represent a closed saccular dilatation of a bronchus or an epithelialized cavity within the lung, produced by necrosis and destruction of lung parenchyma. Extensive interstitial fibrosis. *Left:* greatly thickened pleura of the costal surface.

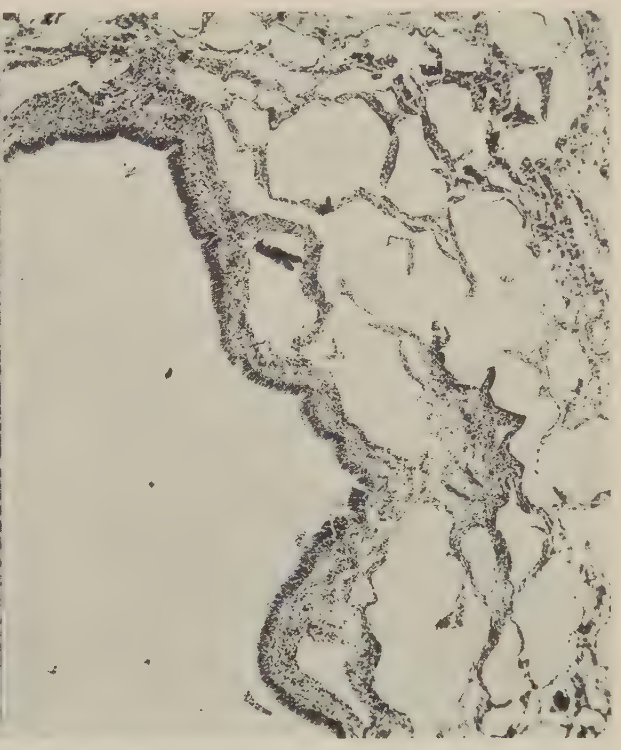
(All from E. Hirsch and P. Holinger, Chicago, Ill.)



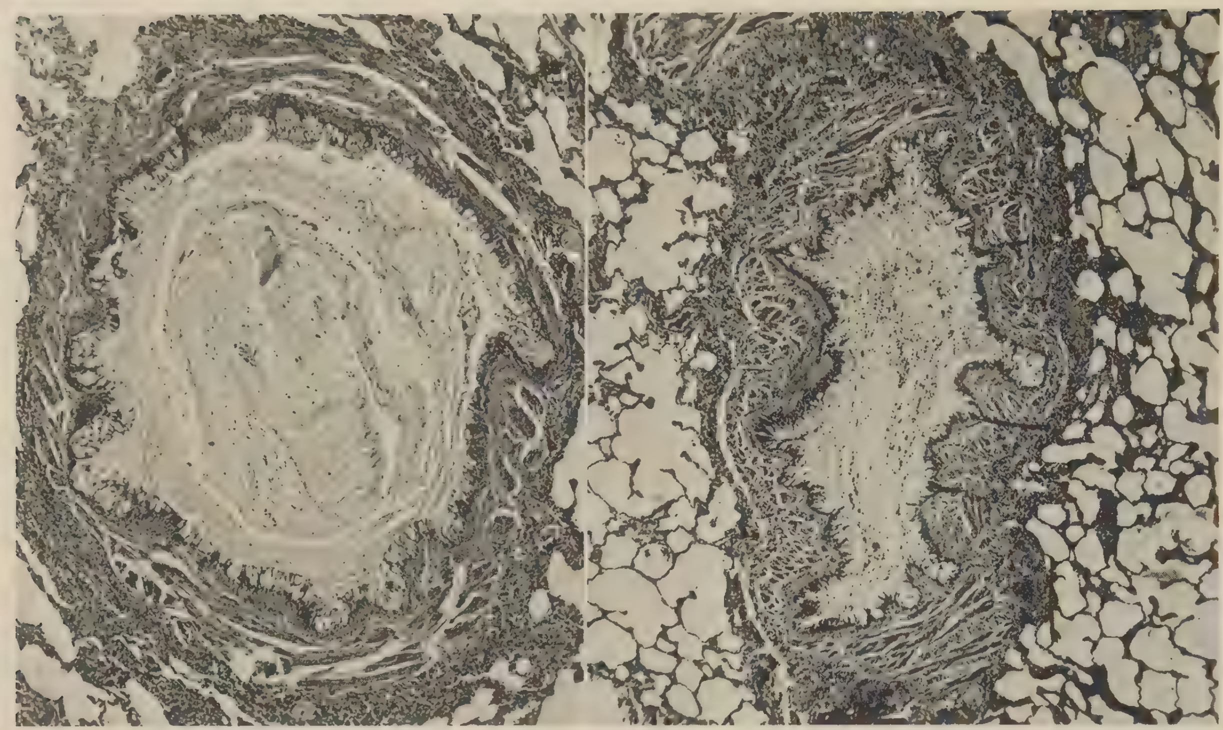
Bronchiectasis, chronic, severe, of left lower lobe in 29 year old man with chronic cough, expectoration and fever for seven months. The enlarged bronchi from the hilus to pleural surface show "cylindrical" and "saccular" dilatations, many containing purulent exudate and bronchiectatic abscesses. No evidence of obstruction. Fibrosis and atelectasis of surrounding lung tissue. *Right:* severe chronic inflammation in walls of enlarged bronchi. x8.



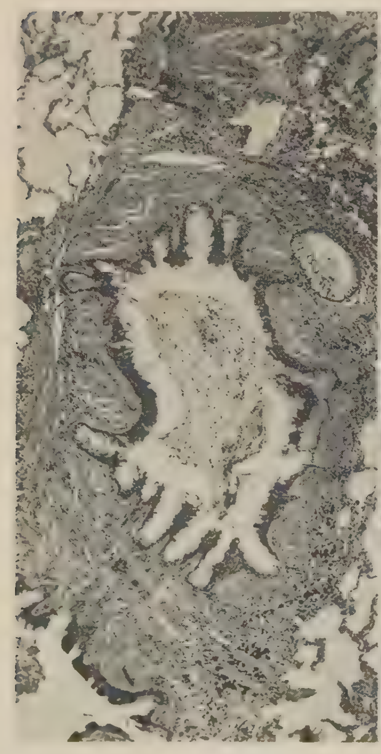
Atelectasis, adjacent to dilated bronchus containing purulent exudate. No muscle or glands in the hyperemic, thickened bronchial wall; dense inflammatory exudate. x48.



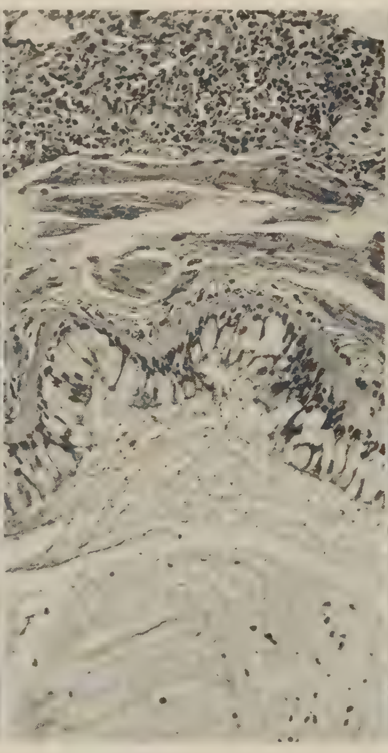
Emphysematous lung parenchyma surrounding part of enlarged bronchus, composed only of thin fibrous wall and hyperplastic respiratory epithelium. x48.



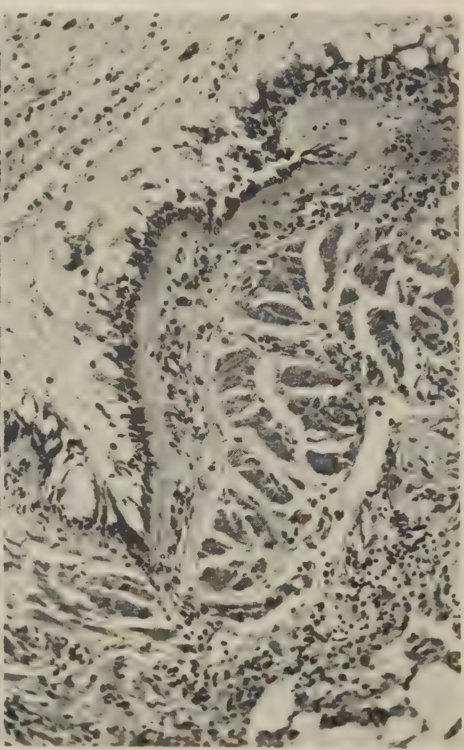
Bronchioles in asthma of many years' duration. Lumens completely occluded by thick, stringy tenacious mucus containing epithelial and inflammatory cells; transformation of respiratory epithelium to an active mucus-producing surface. Mucosa in characteristic folds over apparently hypertrophied smooth muscle layer encircling bronchus and in state of contraction. Edema and fibrosis of thickened wall; exudate, notably dense in outer fibrous layer. Emphysema of adjacent pulmonary parenchyma. x48, x45.



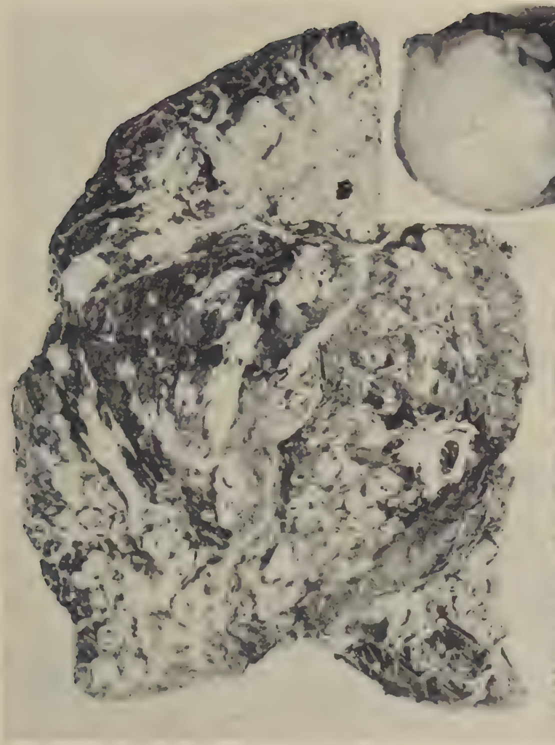
Inspissated mucus plug in smaller bronchiole (Curschmann's spirals in sputum.) x48.



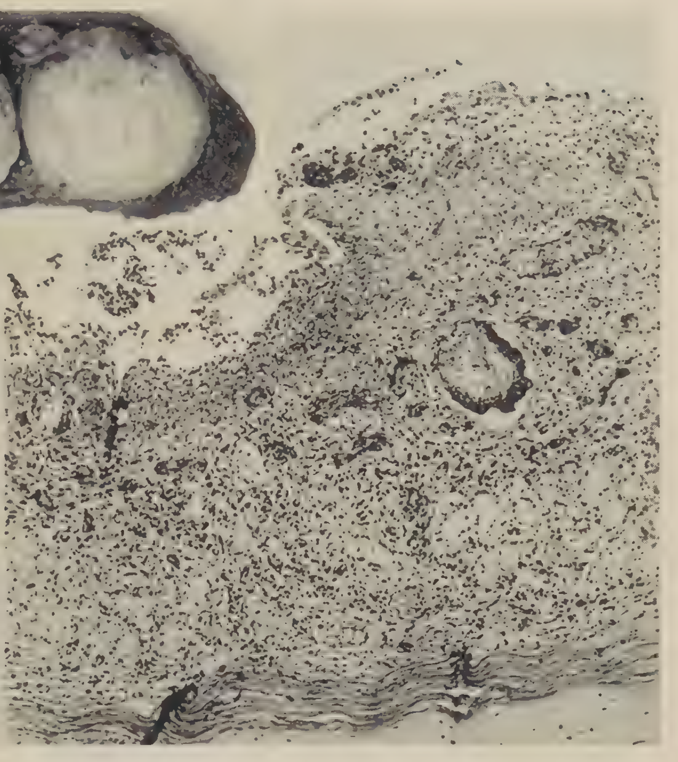
Pure "goblet cell" epithelium producing viscid mucus; edematous wall; exudate. x125.



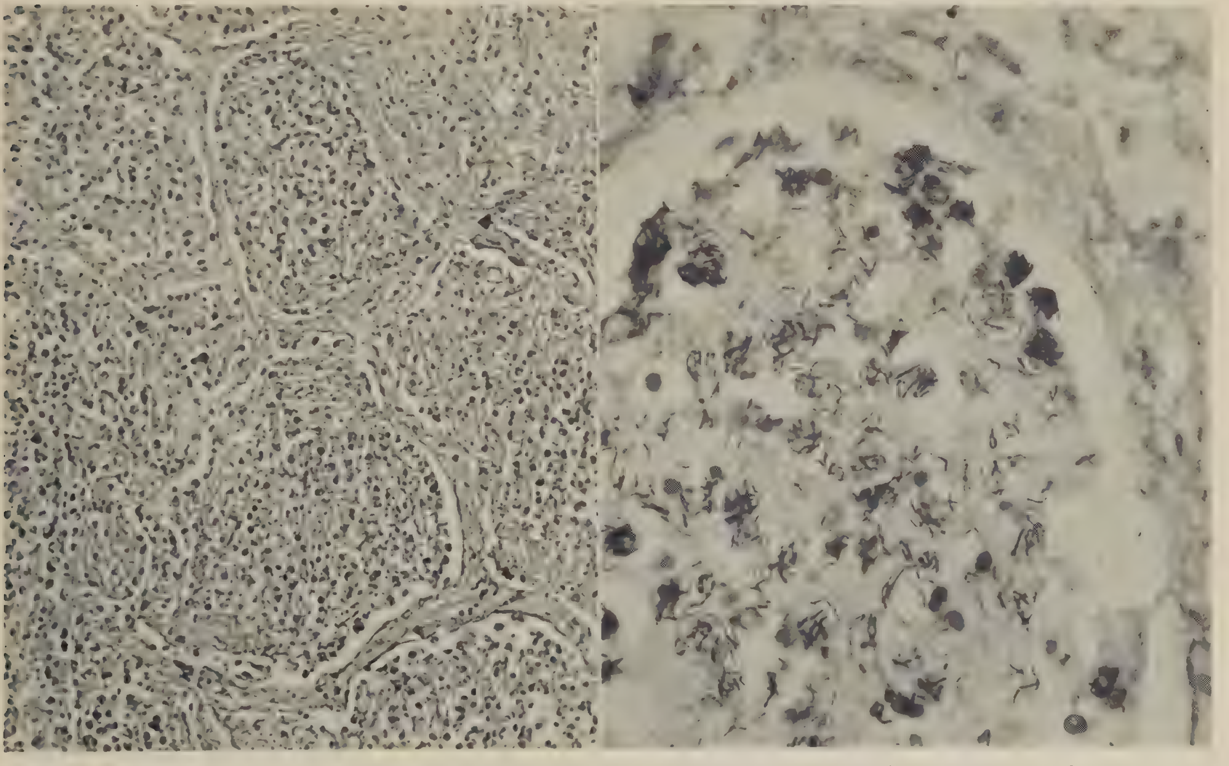
Hyalinized basement membrane; prominent smooth muscle layer; eosinophils, lymphocytes, monocytes in exudate. x160.



Tuberculous bronchitis. Pneumonectomy specimen showing extensive involvement of bronchial tree. Inset: encapsulated caseous tuberculoma removed surgically from lung. (P. Holinger and E. Hirsch).



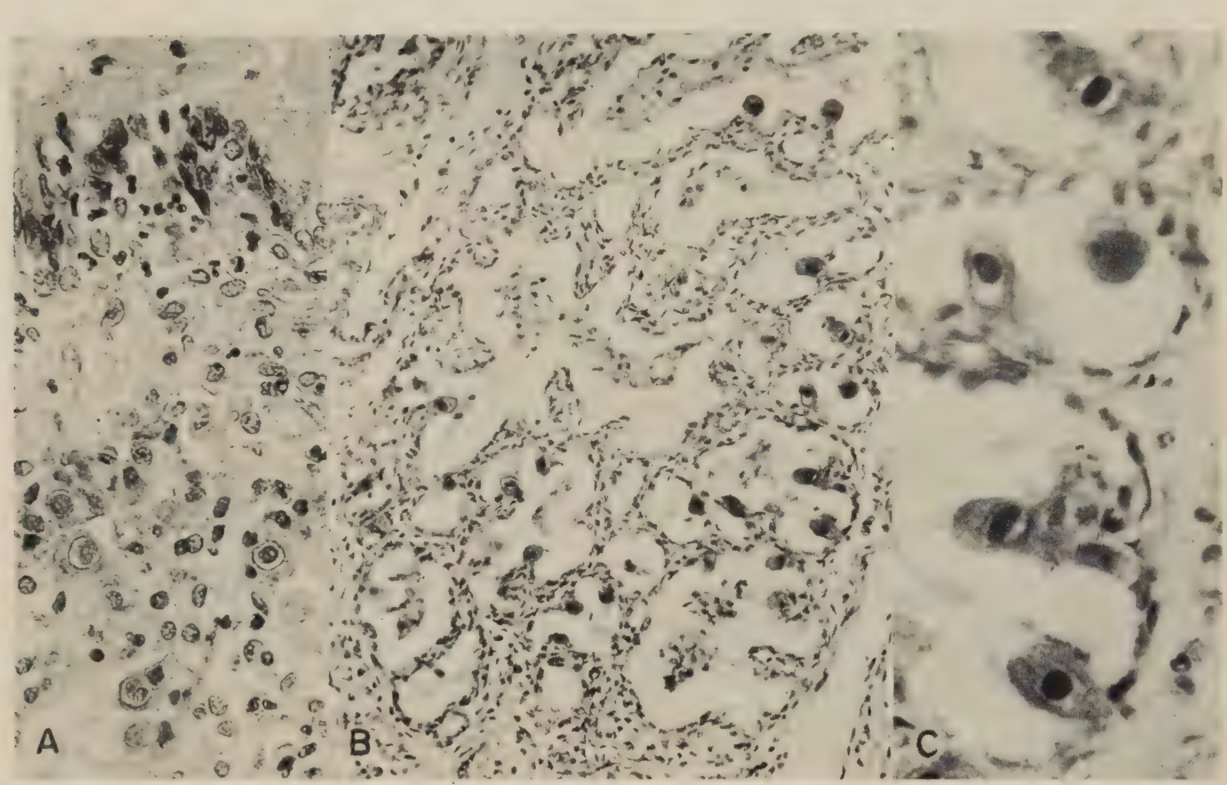
Ulceration of large bronchus in patient with active tuberculosis. Vessels are occluded by fibrin thrombi. Cartilage at bottom. x 83.



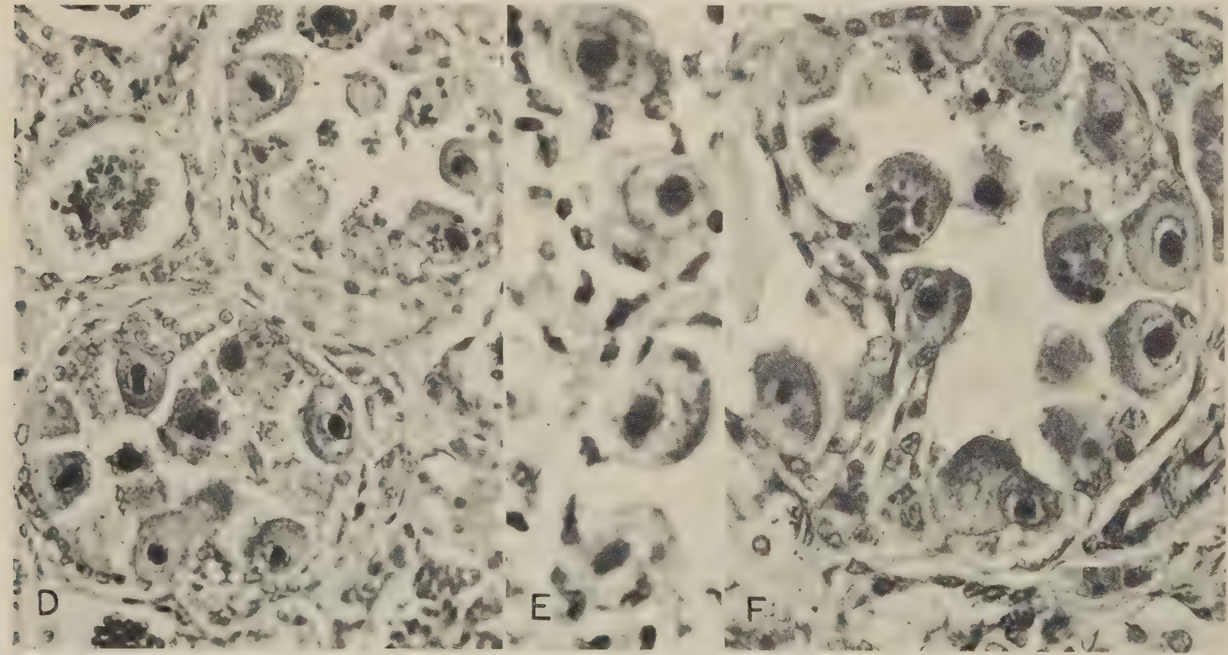
Caseous pneumonia in patient with pulmonary tuberculosis. Terminal exudative reaction to massive infection. Note enormous number of tubercle bacilli in high power from field at left. x 185, x 1000.

CYTOMEGALIC INCLUSION DISEASE

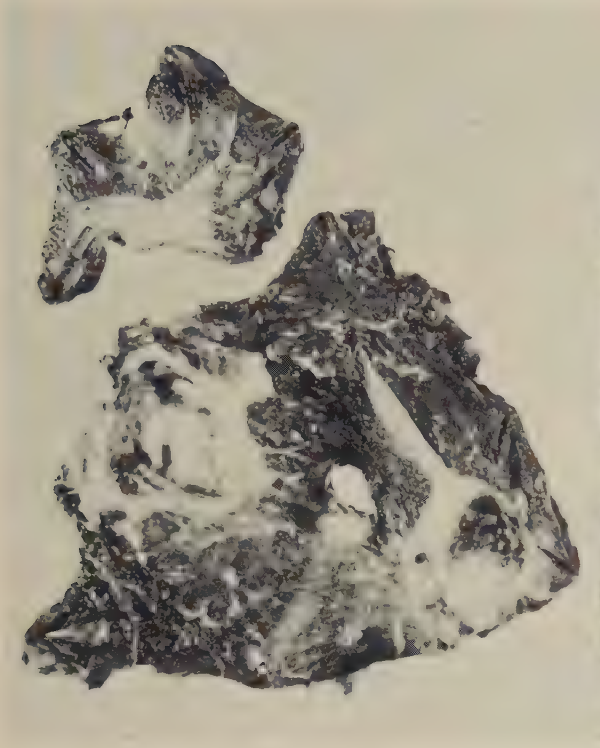
(SALIVARY GLAND VIRUS INFECTION)



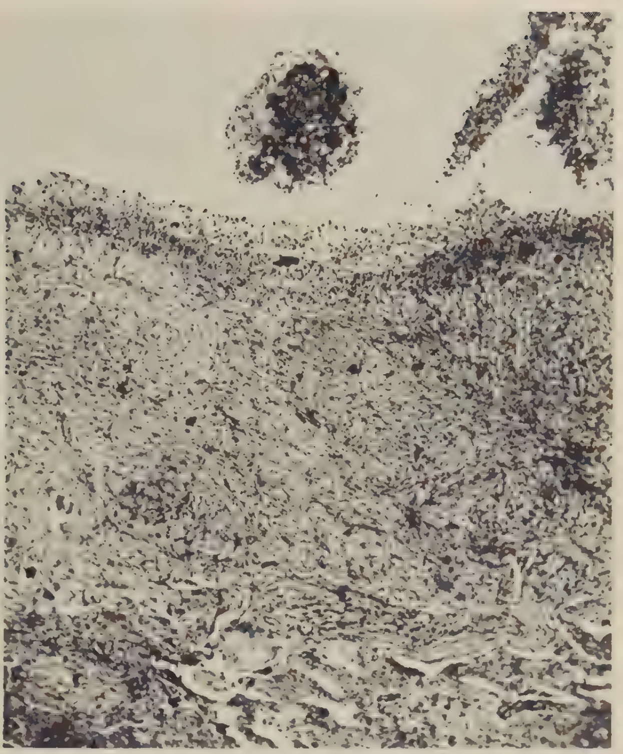
Characteristic inclusions of the salivary gland virus are reported to be demonstrable in the salivary glands of 10 per cent of infants dying of any cause. A generalized infection with this virus is now recognized as a not uncommon cause of deaths in infants. **A.** Inclusions within bronchial lining and gland epithelium in case of a 4 month old baby with an interstitial pneumonia. x230. **B** and **C.** Inclusions apparently present in alveolar duct cells of a 4 month old infant who had had pertussis. x185, x700.



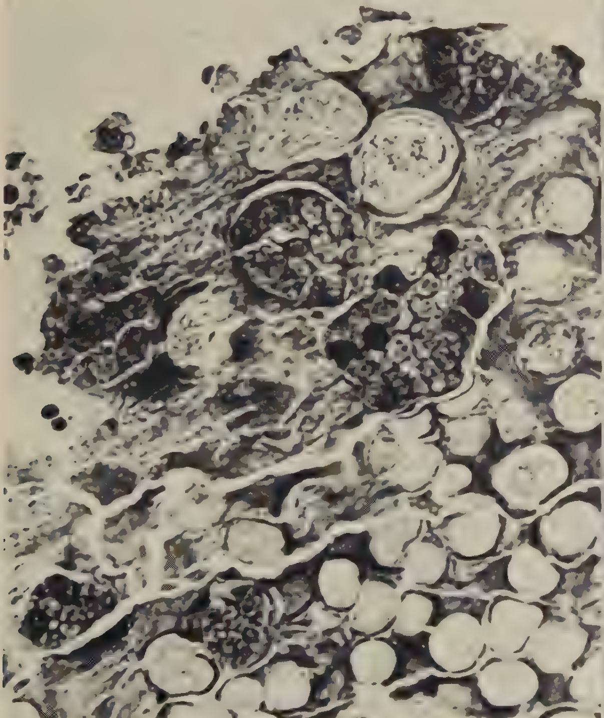
The striking, very large intranuclear inclusions are granular and usually accentuated by a surrounding clear zone. The cytoplasmic inclusions are considerably smaller and less prominent. **D** and **F.** Inclusions in renal tubular epithelium in a premature (7½ month) infant, who lived eight hours. x275, x500. **E.** Higher magnification of inclusions in alveolar duct epithelium. x900.



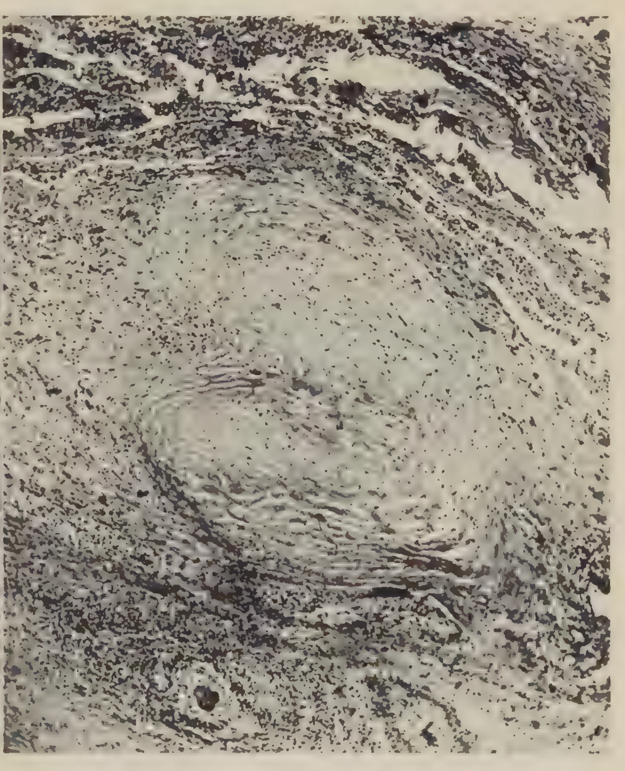
Two pulmonary lesions in wedge resections, from right upper lobe of a young man, contain: a 1 cm. nodule (upper); a bisected 3 cm. mass (lower). Latter has a central 2 cm. cavity, which had been noted in roentgenograms.



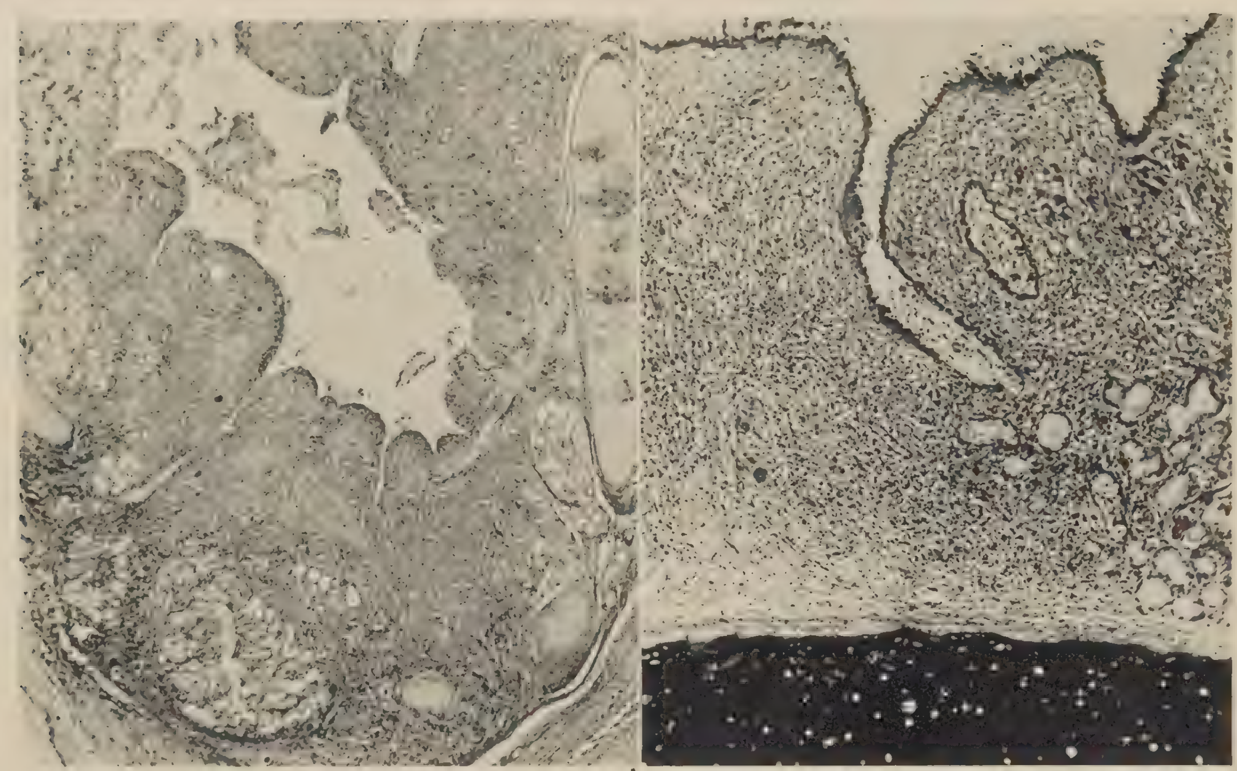
Wall of cavity is composed of dense fibrous tissue with purulent necrotic surface. Dark mass in lumen of cavity at top contains numerous organisms. PAS stain. x55. *C. immitis* identified in preoperative sputum culture.



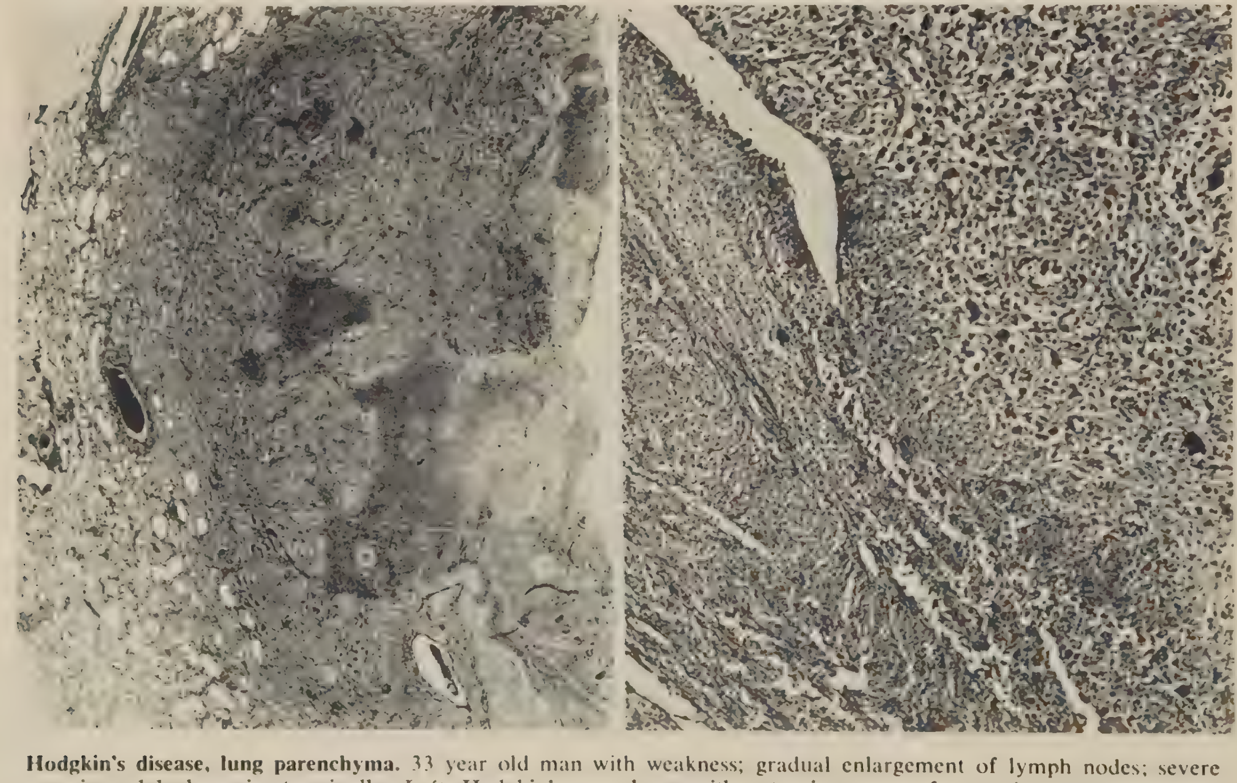
Coccidioides immitis in varying stages of development. Maturing spherules and endosporulating organisms. x500.



Fibrotic tubercle, in upper part of which are giant cells containing an occasional poorly stained organism. x62.



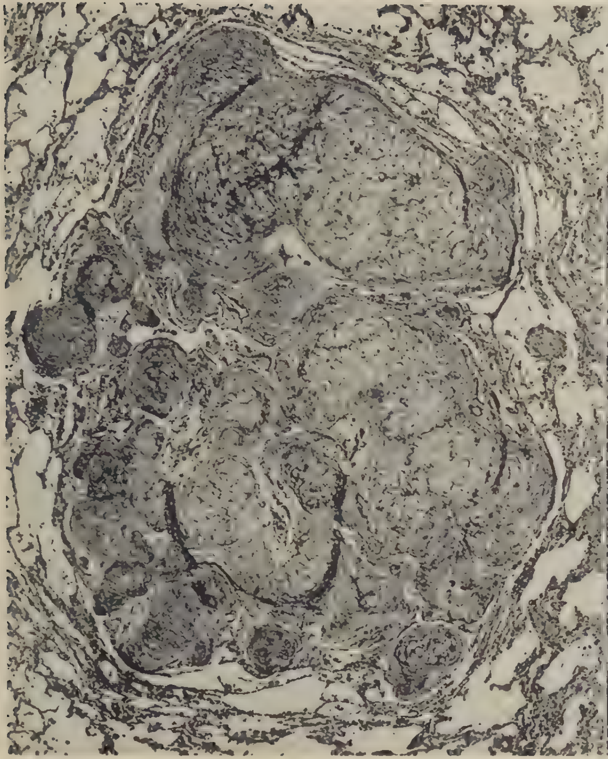
Hodgkin's disease, bronchus. Marked narrowing of the lumen of a large bronchus produced by the greatly thickened mucosa. Note typical diffuse infiltration about mucosal structures and absence of ulceration. x21, x45. Upper respiratory tract mucosa of this young adult was similarly involved.



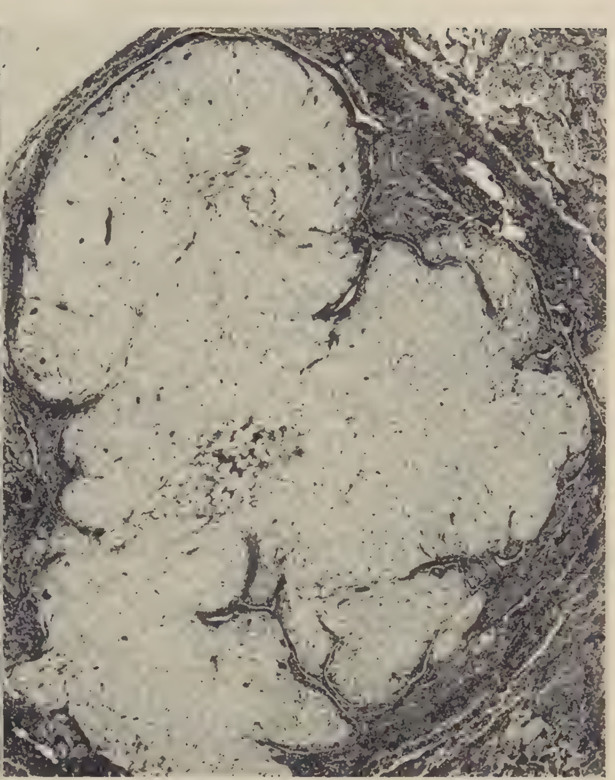
Hodgkin's disease, lung parenchyma. 33 year old man with weakness; gradual enlargement of lymph nodes; severe anemia and leukopenia, terminally. *Left:* Hodgkin's granuloma with extensive areas of necrosis. *Right:* numerous Reed-Sternberg cells in diffusely cellular area adjacent to necrotic focus. x8, x98.

HAMARTOMA, LUNG

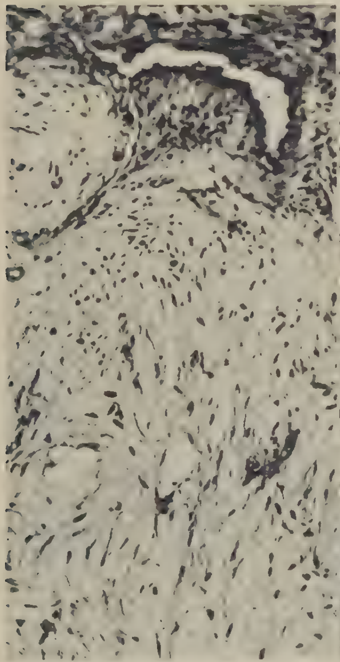
CIRCUMSCRIBED–DIFFUSE



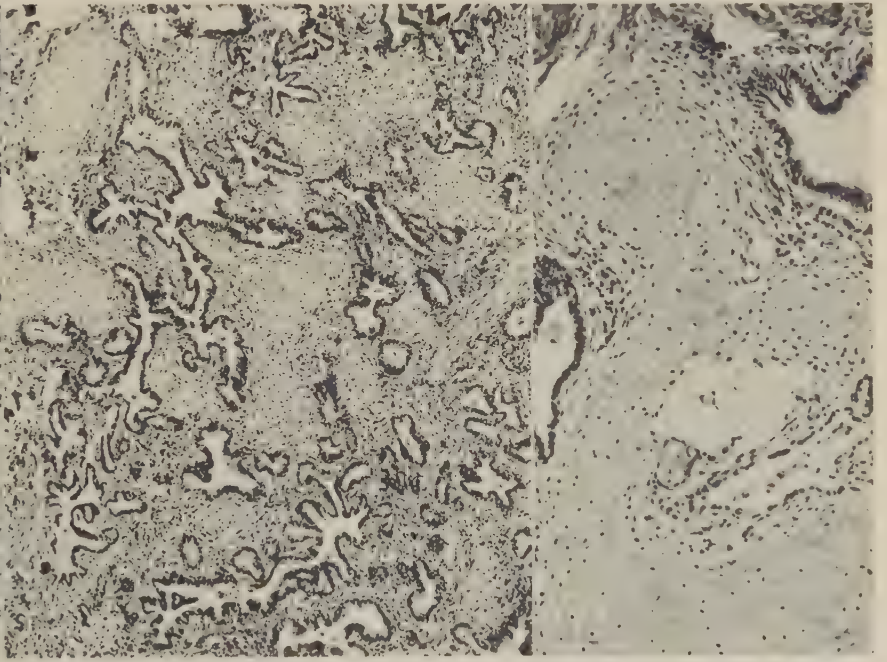
Hamartoma, chondromatous. Circumscribed mass in periphery of right upper lobe of a 54 year old man, produced no symptoms. Well differentiated fibrocartilage; clefts lined by cuboidal and columnar epithelium. x24.



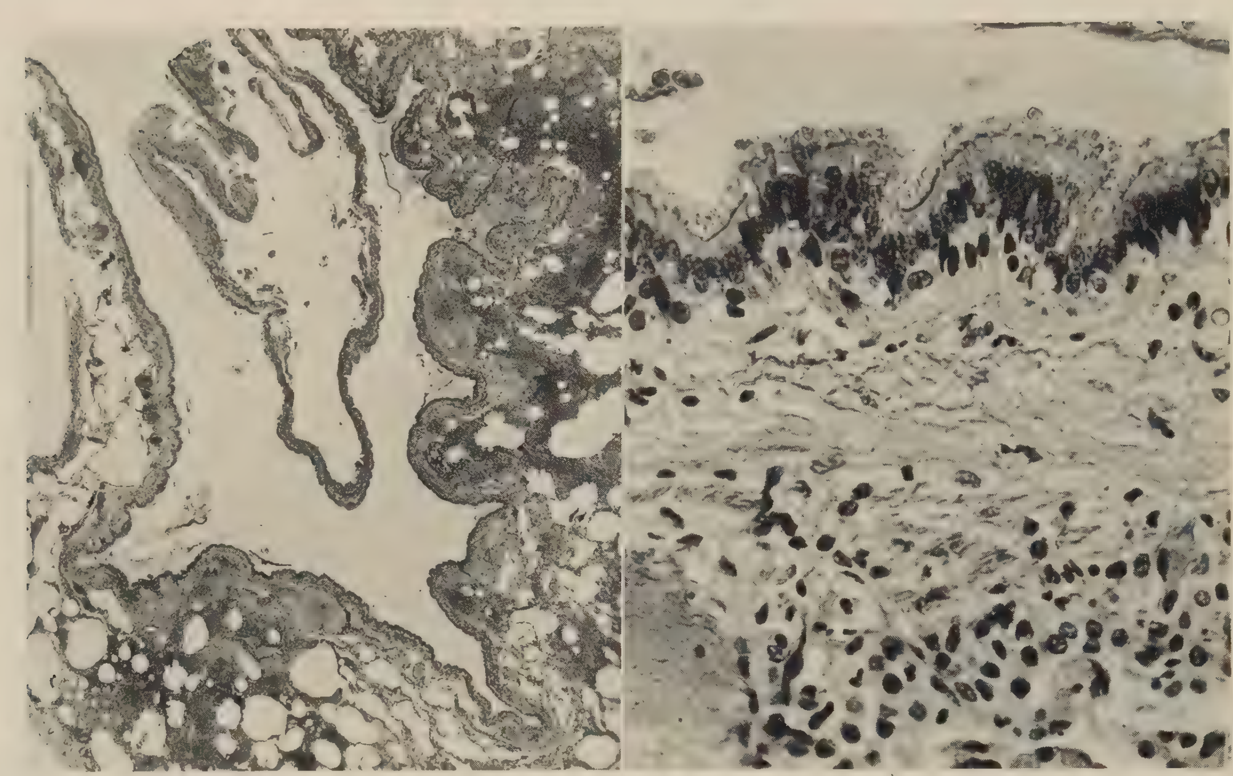
Hamartoma, myxofibrolipomatous. Incidental autopsy finding in 59 year old man. Well circumscribed subpleural tumor. Fibromyxomatous stroma; collections of fat cells; flattened epithelium lining clefts. x28.



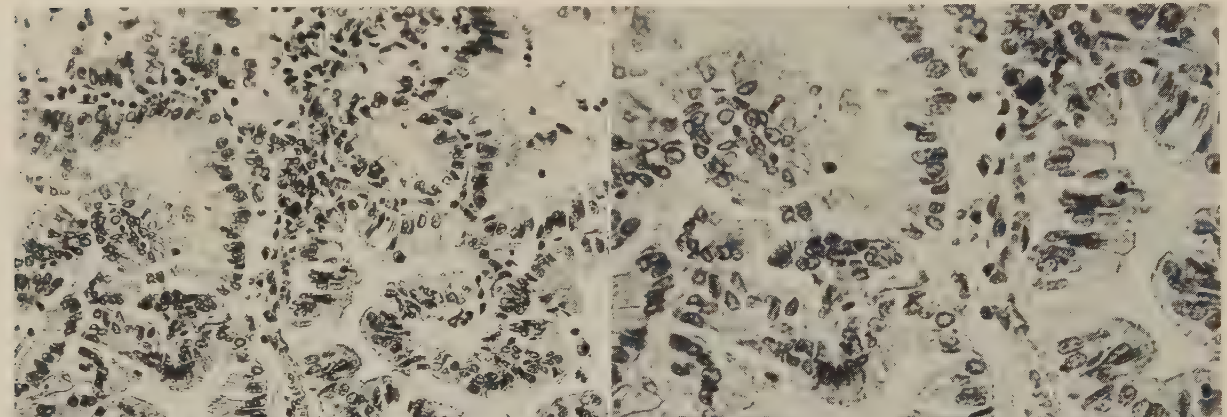
Magnified field from tumor in *upper right* figure. Spindle and stellate cells with long, delicate fibrous processes. x125.



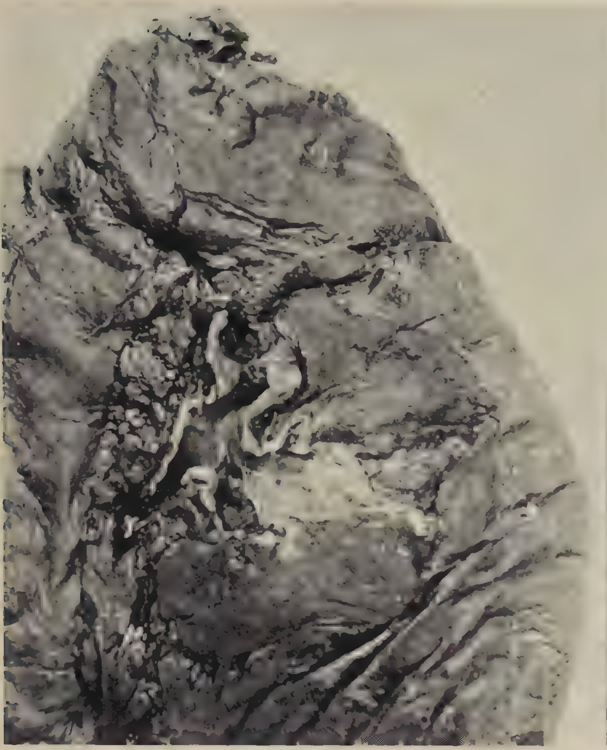
Hamartoma, adenochondromatous, diffuse type. Multiple lesions which were not circumscribed or encapsulated in resected lower lobe of left lung of a 19 year old Negro male. Cuboidal, columnar, or respiratory epithelium lines branching spaces; islands of well-differentiated hyaline cartilage; strands of smooth muscle; groups of fat cells. "An abnormal mixing of normal components" of the bronchus. x57; x125.



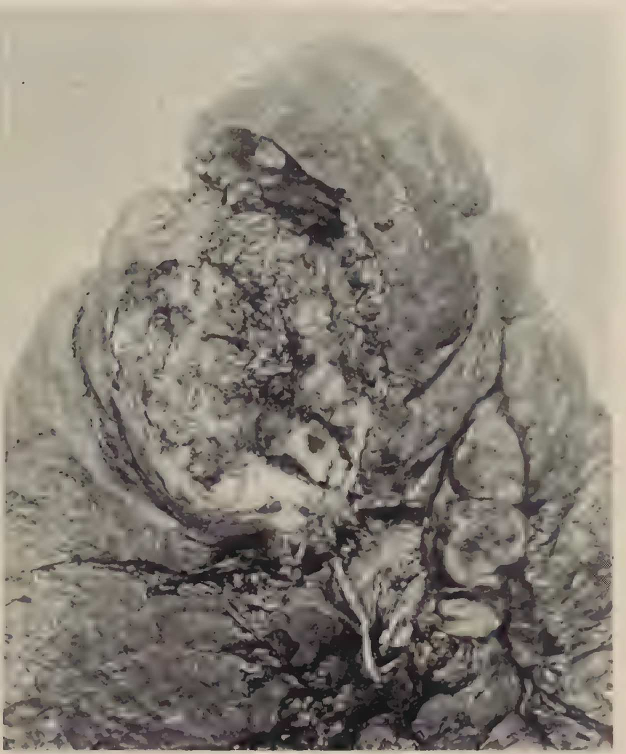
Bronchogenic cyst, right lower lobe of a 22 year old man. On operative removal, no connection with bronchus was evident. Cyst, 3 cm. in diameter, lined by well differentiated ciliated pseudostratified epithelium, normal in upper respiratory tract. x 14, x 330.



Pulmonary adenomatosis of a type resembling jaagziekte, common in lungs of sheep. The present tendency is to group this rare pulmonary disease with the bronchiolar cell carcinomas. x 270, x 355.

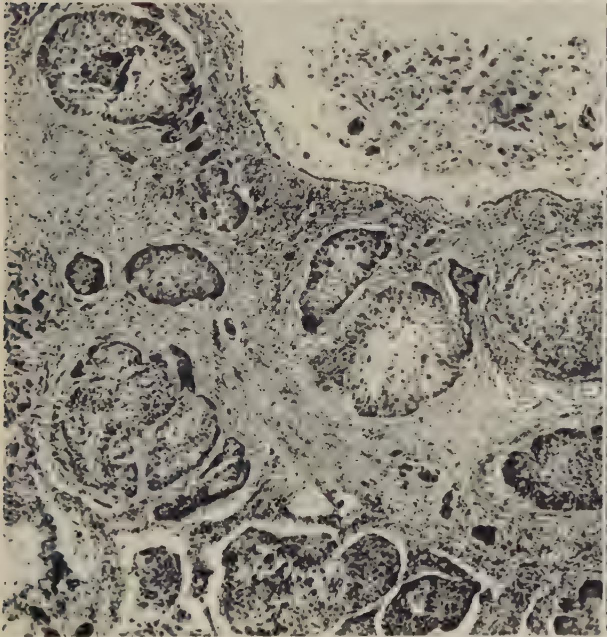


Pneumonectomy specimen: epidermoid carcinoma of right middle lobe bronchus in a 50 year old man with hoarseness, cough and hemoptysis of only ten days' duration. Tumor occluded lumen and extended into its medial and lateral branches. Atelectasis of adjacent lung parenchyma.

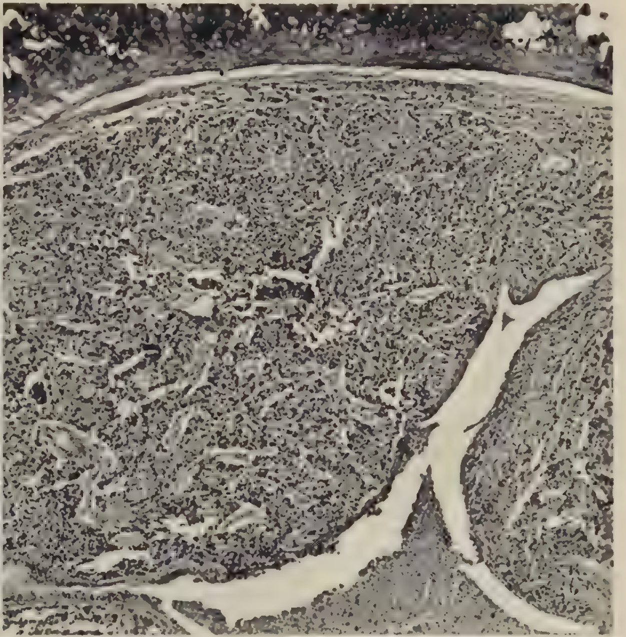


Pneumonectomy specimen: undifferentiated carcinoma evident as white thickening occluding right upper lobe bronchus of 50 year old man. Pneumonitis, suppuration and necrosis of lung segment distad. History of cough, hemoptysis, chest pain three months previously.

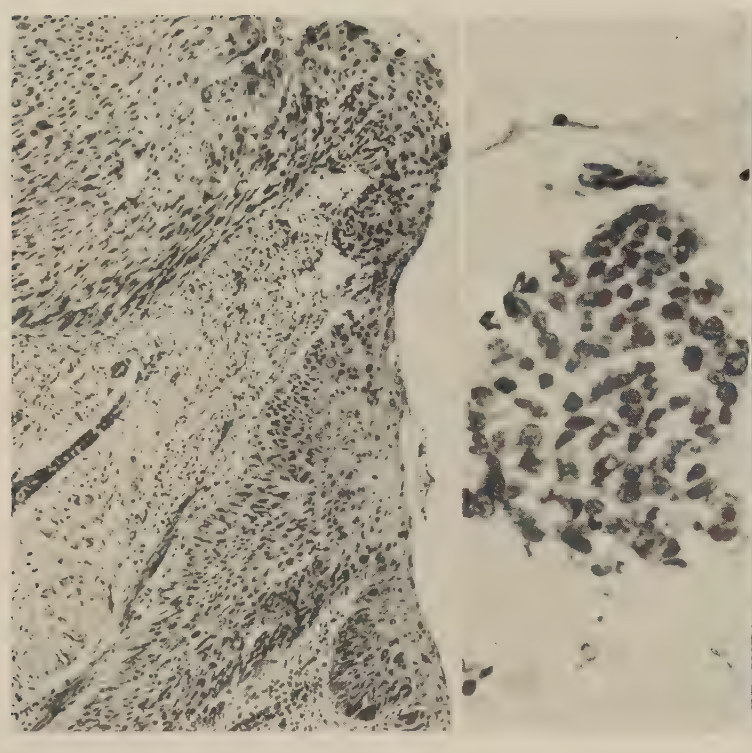
(Both from P. Holinger and E. Hirsch, Chicago, Ill.)



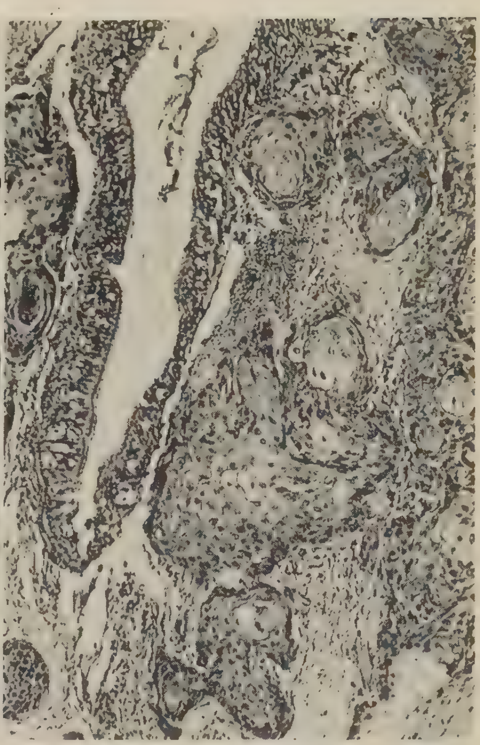
Secondary extension of epidermoid carcinoma of a large bronchus to pulmonary alveoli and the mucosa of an adjacent bronchus.



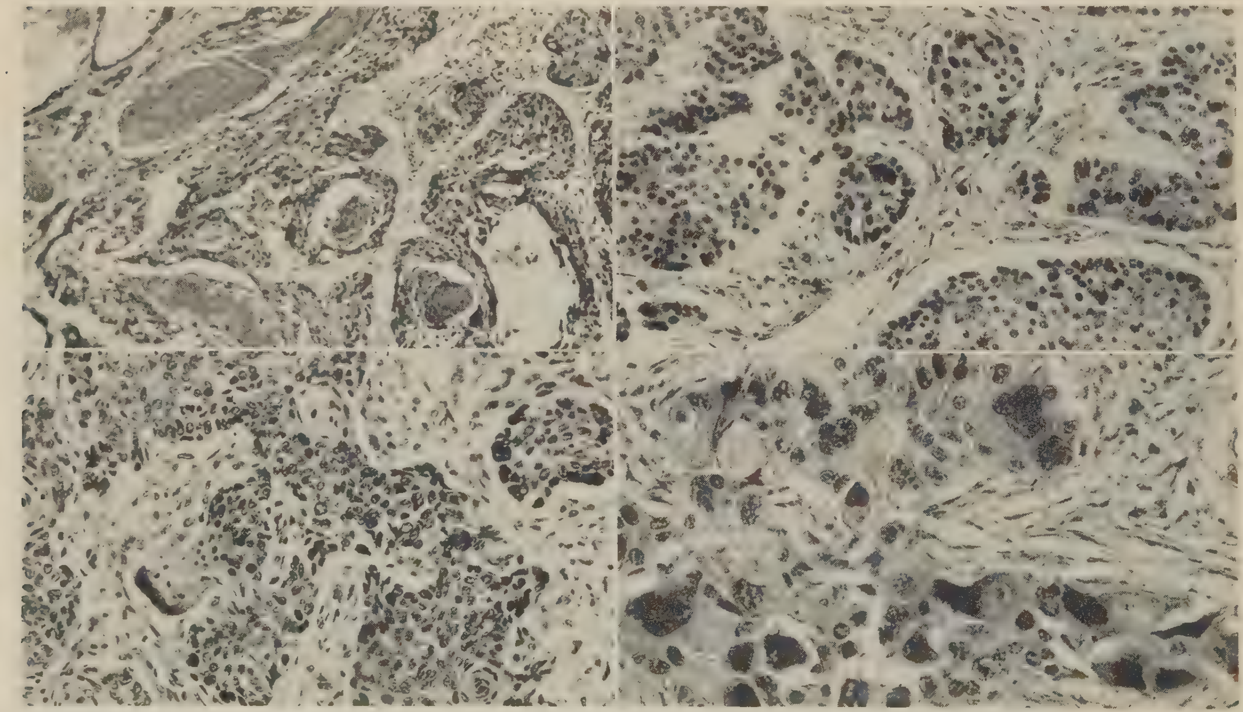
Virtual occlusion of lumen of large bronchus adjacent to main tumor mass by mucosal invasion of undifferentiated small cell carcinoma. x36.



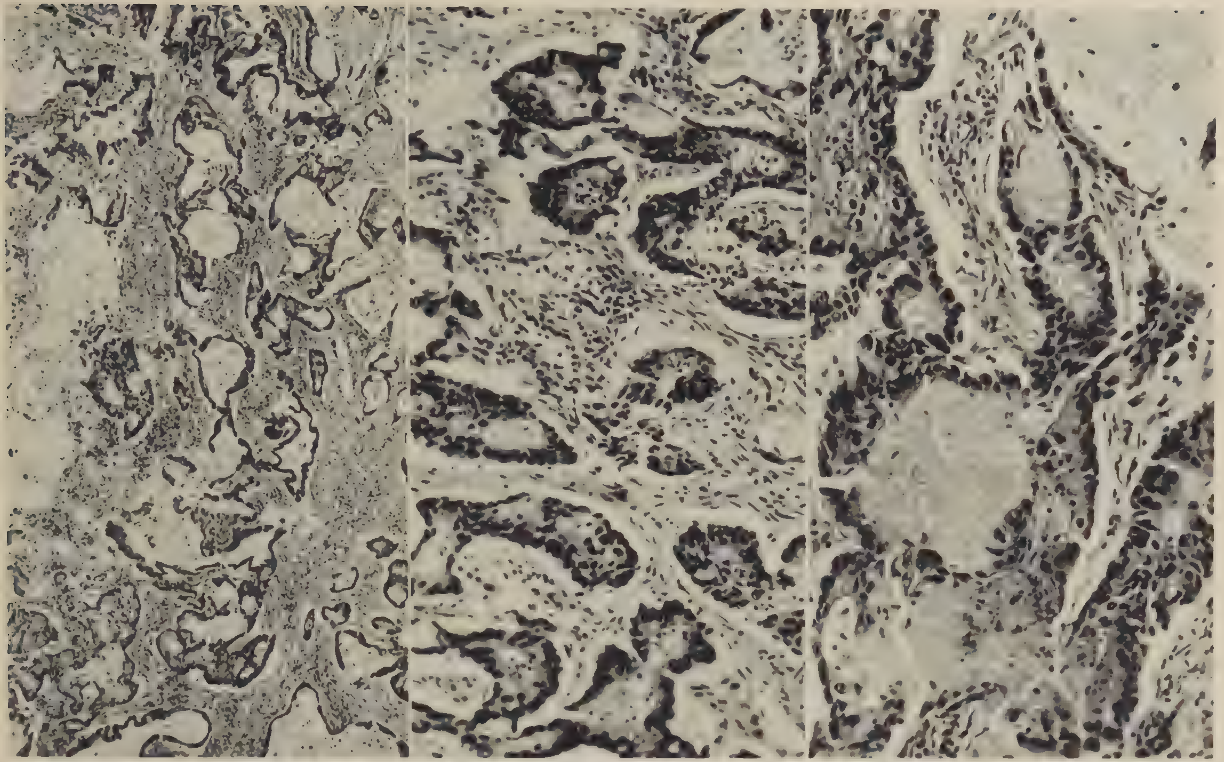
Smears for cytologic examination of bronchial secretions before pneumonectomy contained malignant cells such as cluster at *right* with 4 in mitosis. Extensive area of malignant dyskeratosis ("carcinoma in situ") in left lower lobe bronchus was presumably the source *(left)*. A "silent" adenocarcinoma was found in upper lobe. x90, about x150.



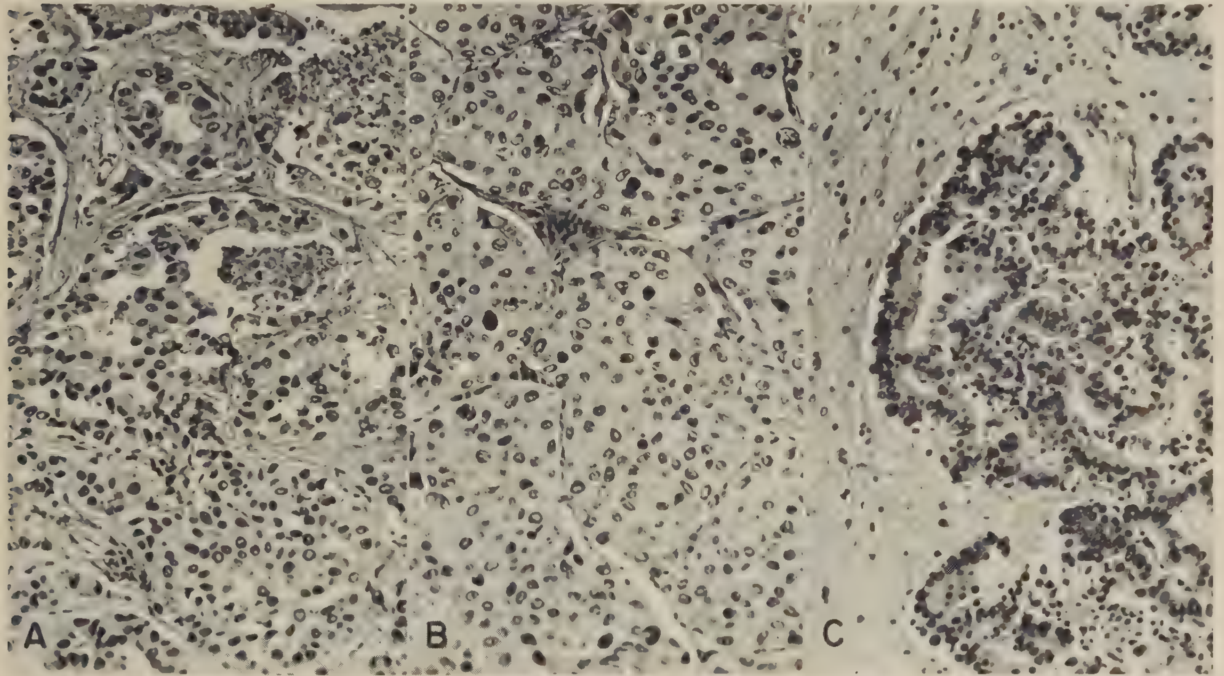
Bronchoscopic biopsy specimen from orifice of left upper lobe bronchus. Well differentiated epidermoid carcinoma beneath intact mucosal epithelium. x90.



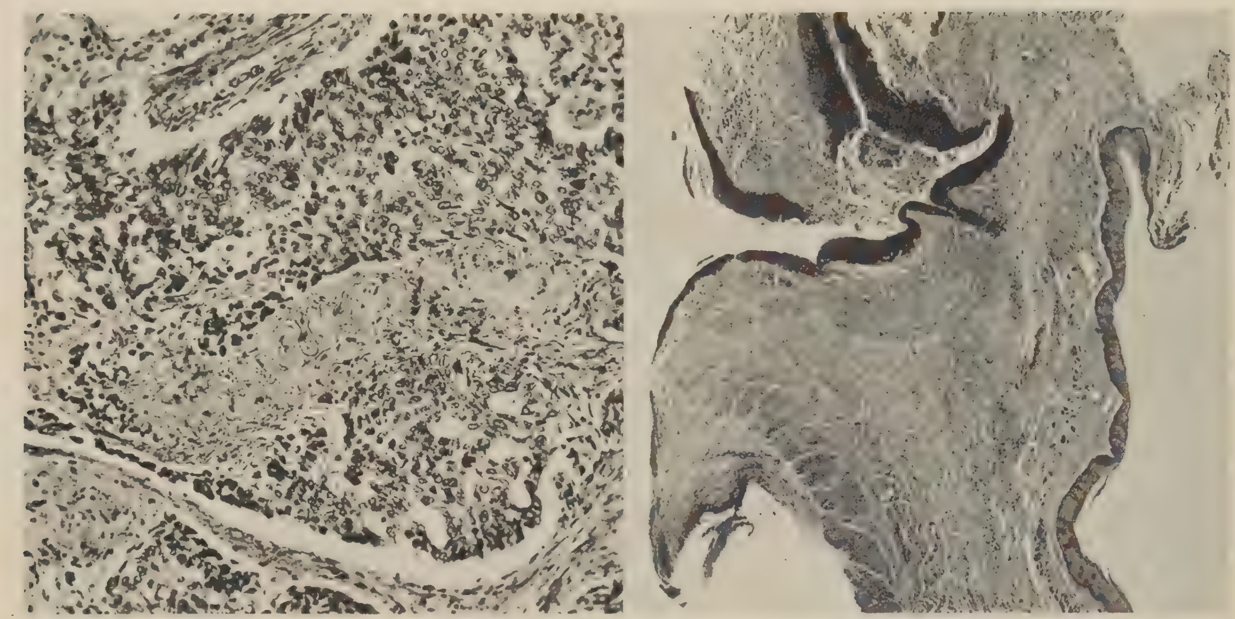
Epidermoid carcinoma of lung. *Upper left:* well differentiated, keratinizing carcinoma with epithelial pearls. x76. *Lower left:* less differentiated carcinoma with small foci of keratinization. x125. *Upper right:* poorly differentiated tumor with no keratinization. x150. *Lower right:* pleomorphic epidermoid carcinoma with multinucleated giant cells and bizarre forms. x150.



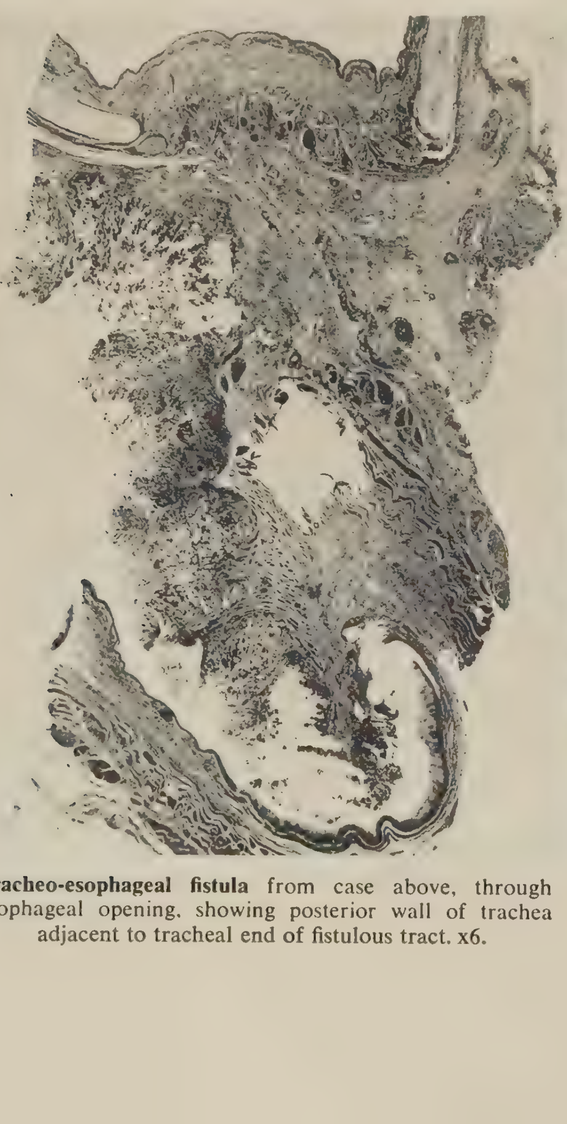
Adenocarcinoma, well differentiated. Adenomatous elements containing mucicarmine-positive secretion from left lung of a 63 year old white man. x48, x125, x185. Since an episode of pneumonia at the age of 19 he had had a productive cough, and later recurrences left him with dyspnea on exertion. In the last year dyspnea had been more frequent, with occasional pain high in the anterior chest on the left side.



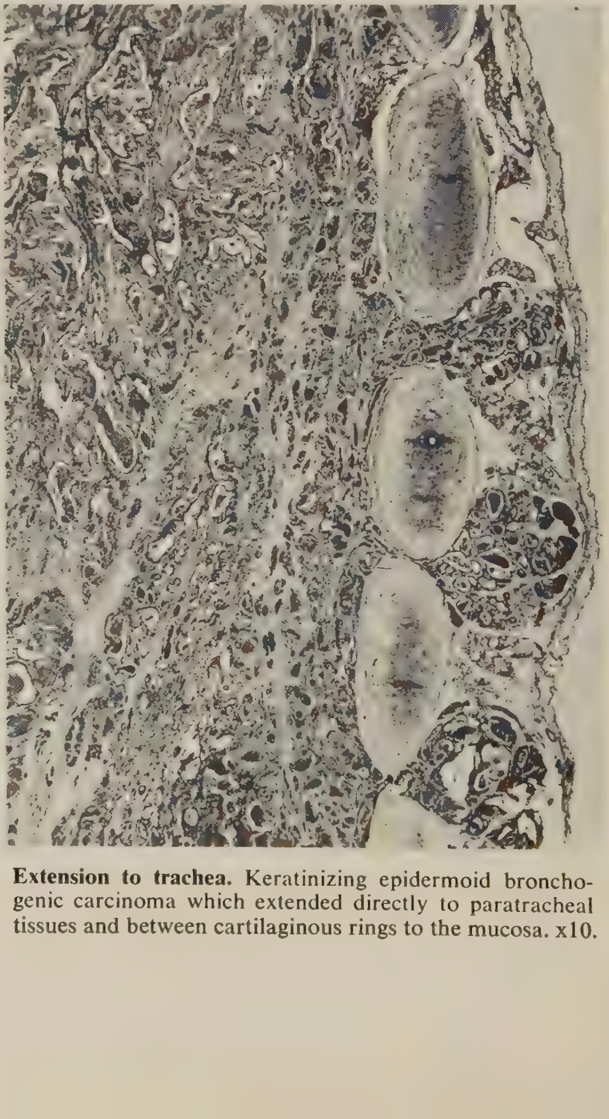
Adenocarcinoma with epidermoid features. A. Moderately well differentiated adenocarcinoma. x125. **B.** Large solidly cellular areas showing squamatoid differentiation in same tumor. x125. **C.** Brain metastasis was better differentiated than the primary tumor. x125. Other sites of metastasis in this 59 year old man were lymph nodes, liver, adrenals, and bone marrow.



Extension to mediastinum. *Left:* bronchogenic carcinoma, mixed epidermoid and adenomatous features, which extended to mediastinal structures and produced a tracheo-esophageal fistula. x125. *Right:* esophageal end of fistulous tract, with necrotic tumor (top) interrupting all coats. x8.

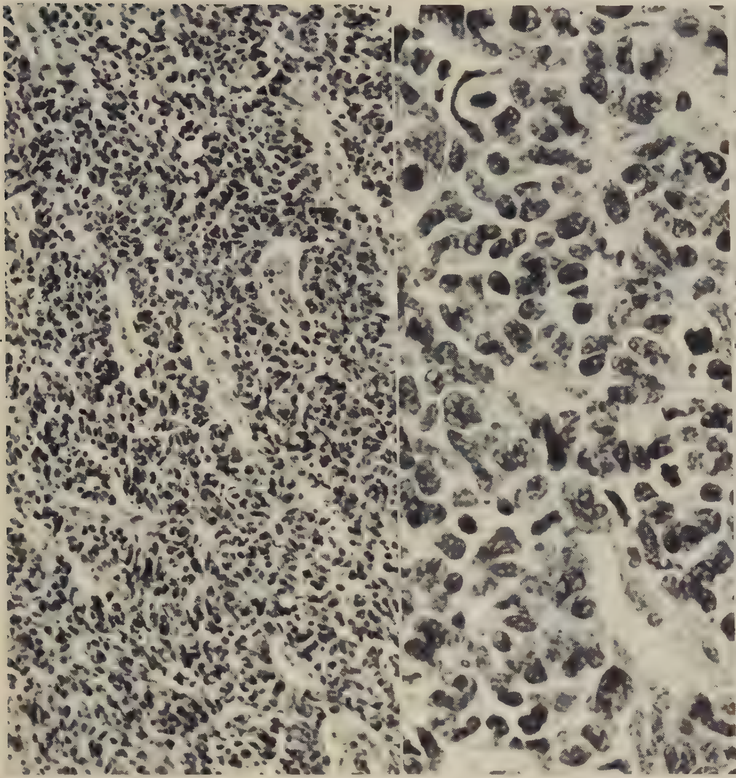


Tracheo-esophageal fistula from case above, through esophageal opening, showing posterior wall of trachea adjacent to tracheal end of fistulous tract. x6.

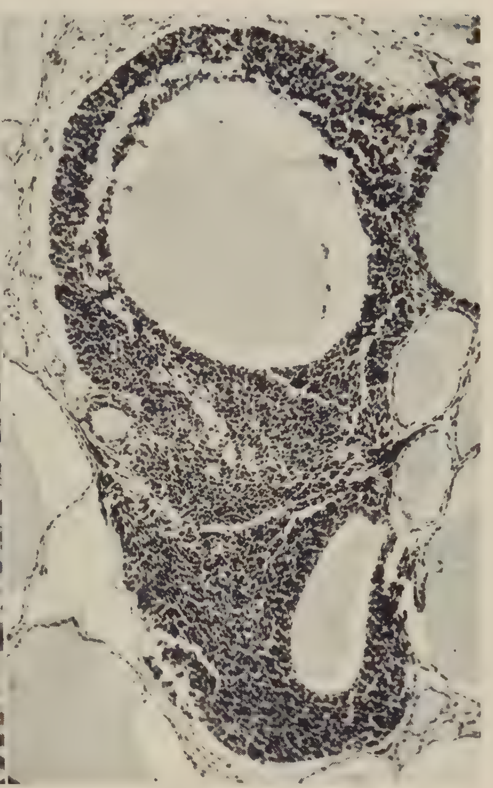


Extension to trachea. Keratinizing epidermoid bronchogenic carcinoma which extended directly to paratracheal tissues and between cartilaginous rings to the mucosa. x10.

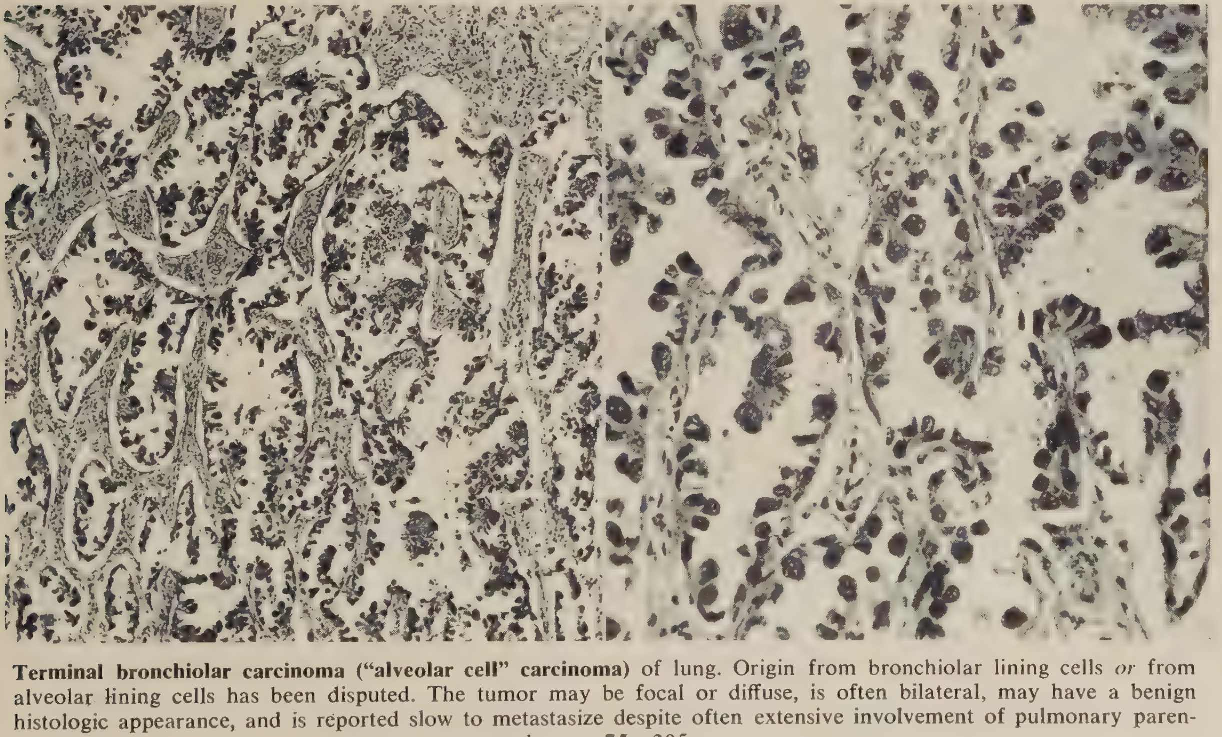
ANAPLASTIC BRONCHOGENIC CARCINOMA
BRONCHIOLAR CARCINOMA



Anaplastic carcinoma, primary in bronchus. Cells are undifferentiated and, in this example, generally large with large vesicular or hyperchromatic nuclei. Very frequent mitoses, some abnormal. x125, x400.

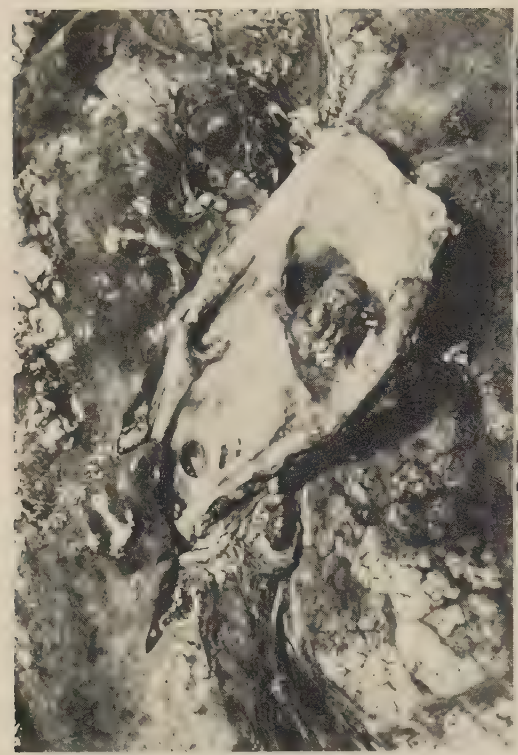


"Oat cell" carcinoma, metastatic in thyroid. Undifferentiated cells are small and tend to be spindle shaped. Patient died with widespread metastases. x125.

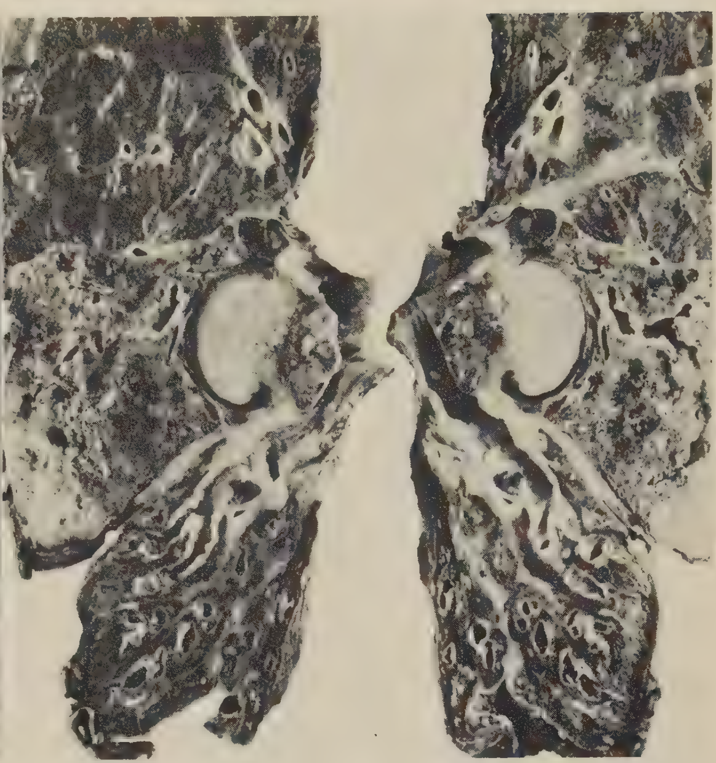


Terminal bronchiolar carcinoma ("alveolar cell" carcinoma) of lung. Origin from bronchiolar lining cells *or* from alveolar lining cells has been disputed. The tumor may be focal or diffuse, is often bilateral, may have a benign histologic appearance, and is reported slow to metastasize despite often extensive involvement of pulmonary parenchyma. x75, x205.

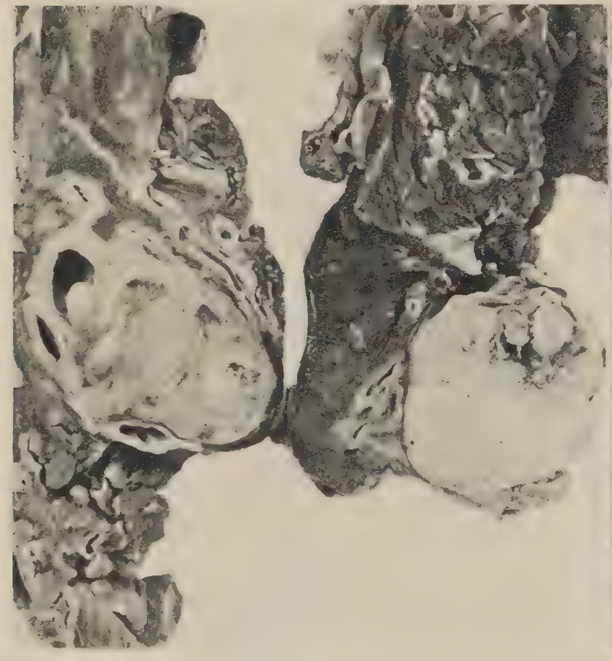
GROSS FEATURES



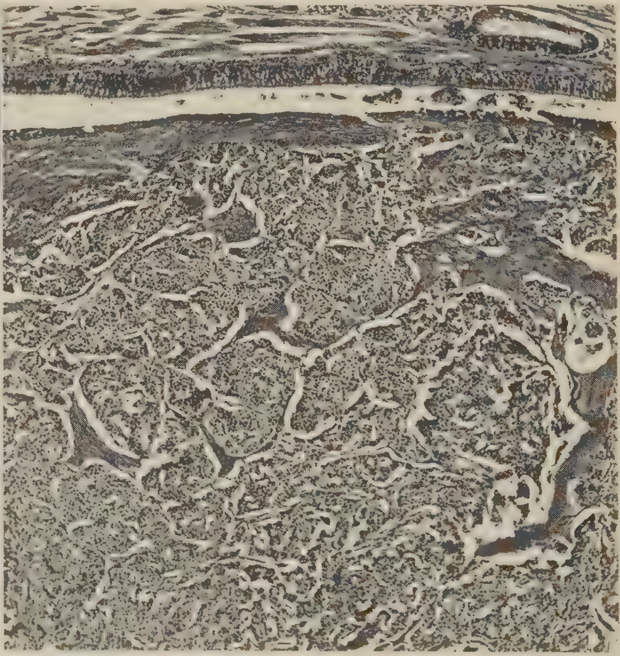
Adenoid cystic carcinoma ("cylindroma"; bronchial "adenoma"), left main bronchus of a 38 year old white man. Gross structure similar to adenoma of "carcinoid" type.



Bronchial adenoma, "carcinoid" type. Typically globoid, broad-based adenoma almost completely occluding enlarged bronchial lumen. Its smooth surface is covered by intact epithelium-lined bronchial mucosa. Note distal bronchiectasis.

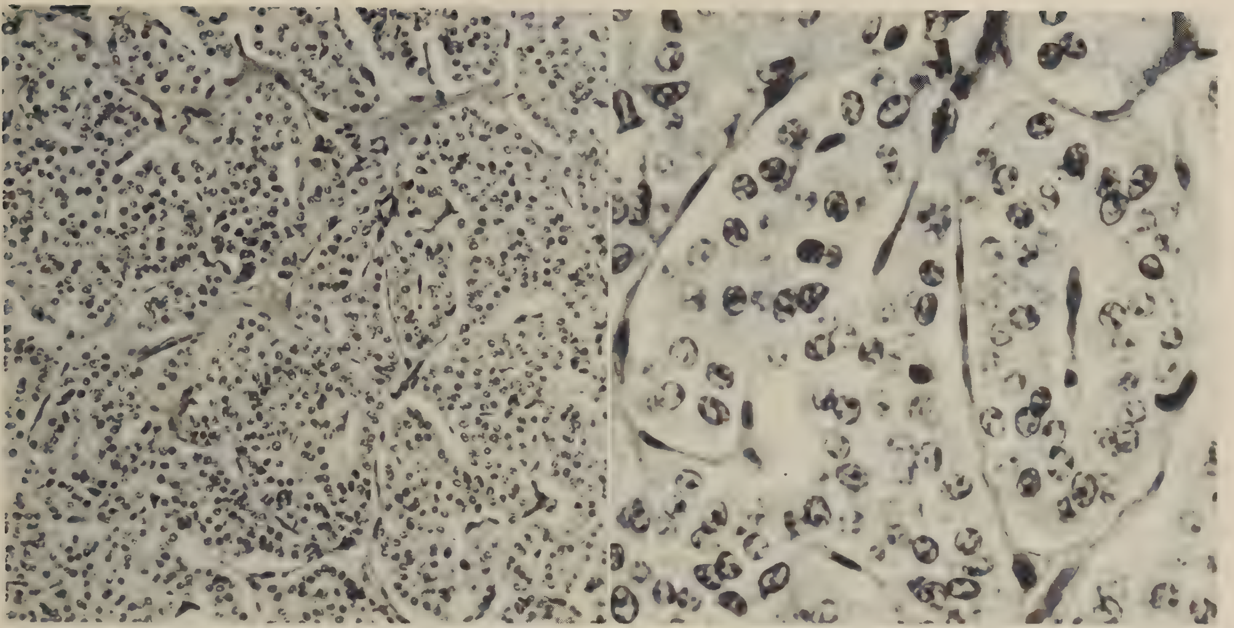


Adenoma of "carcinoid" type, 4 cm. in diameter, with tan homogeneous cut surface, filling lower lobe bronchus. Right lower lobectomy specimen from a 38 year old white man with persistent cough and hemoptysis; atelectasis of right lower lobe in roentgenograms.

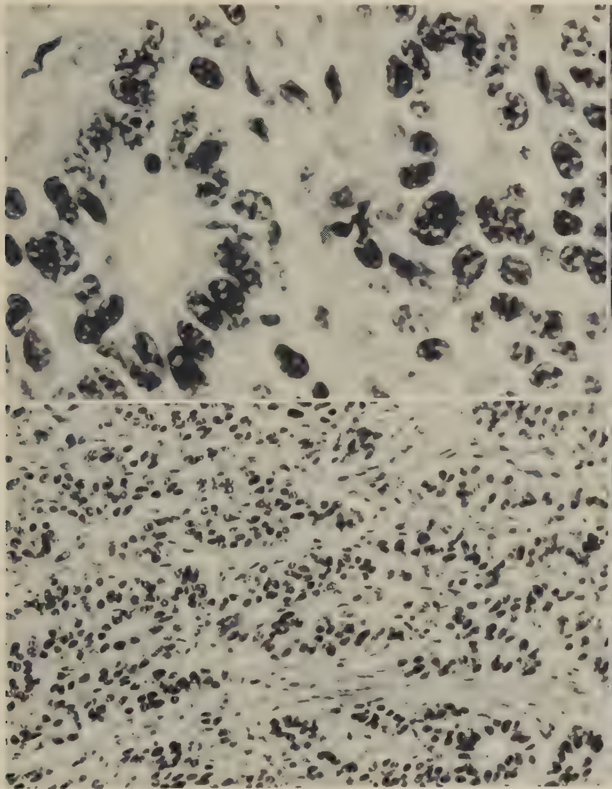


Adenoma almost obliterating bronchial lumen in section from same tumor. Subepithelial band of fibrous tissue covered by thinned but intact epithelium on surface of tumor, and ciliated respiratory epithelium of normal thickness on apposed surface. x48. Details, next plate.

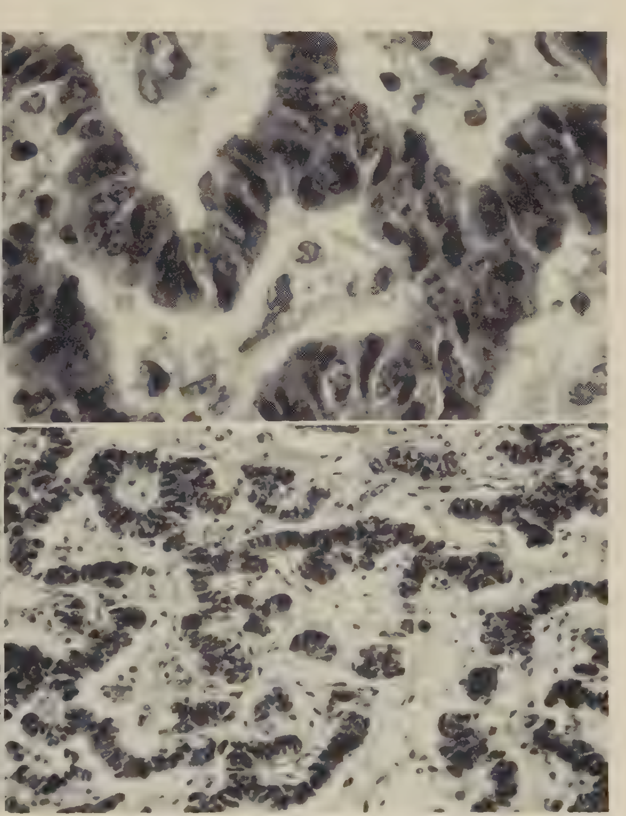
BRONCHIAL "ADENOMA"
"CARCINOID TYPE"



Typical "carcinoid" pattern in adenoma shown at bottom of preceding plate. Nests and strands of small uniform cells with finely granular cytoplasm separated by delicate fibrovascular septa. The latter occasionally form the central core of a grouping, giving pseudoglandular appearance. The round or oval nuclei contain a moderate amount of chromatin, usually finely stippled. No mitoses in these fields. x150, x600.



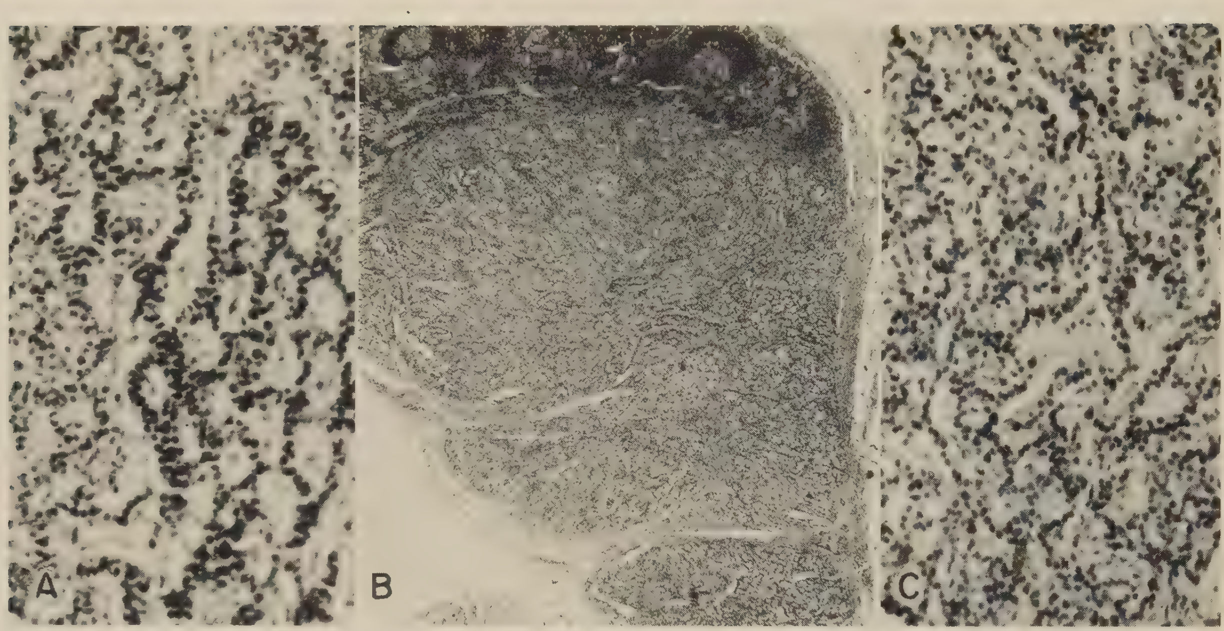
More diffuse pattern with poorly defined cords and occasional well defined glands. Fields selected to include true acini, reported to be an uncommon feature. x600, x150. 38 year old man who died following operation.



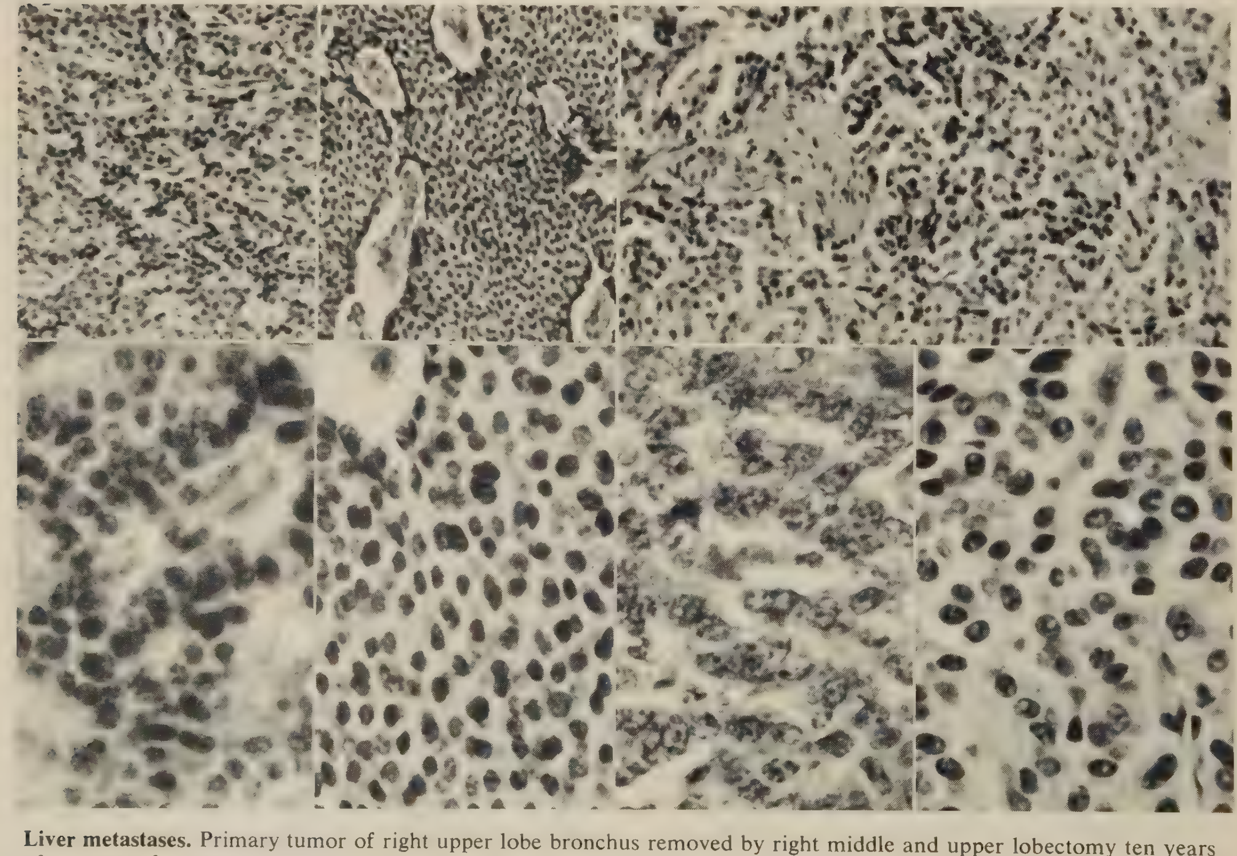
Interlacing cord pattern with considerably more cellular variation in tumor from 37 year old woman with hemoptysis for eight years. Alive and well ten years after pneumonectomy. x600, x150.

BRONCHIAL ADENOMA

CARCINOID TYPE WITH METASTASIS



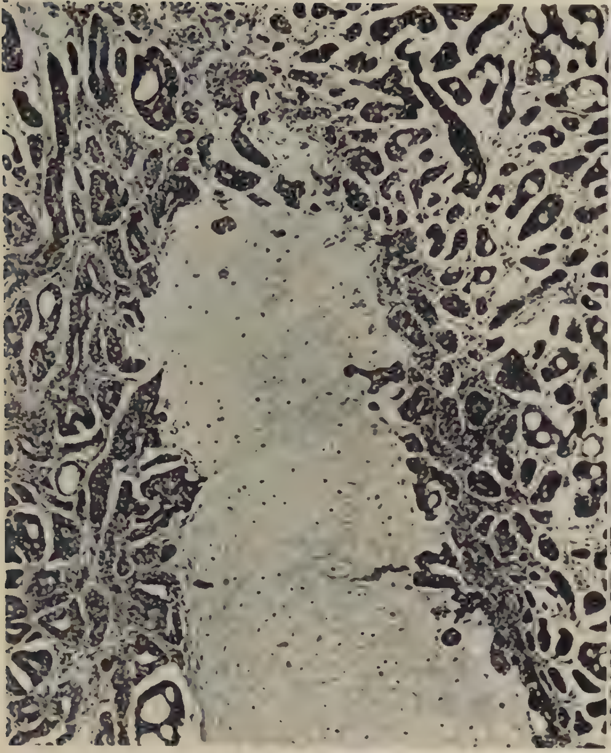
Hilar lymph node metastasis in pneumonectomy specimen from a 32 year old woman with tumor (carcinoid); 4 cms. in diameter, occluding right lower lobe bronchus. Patient was alive and well fifteen years after operation. B. The tumor has replaced most of the lymph node, only a few normal follicles remaining. x 48. The primary tumor, A, and lymph node metastasis, C, have identical patterns and uniform cell type. Both x 185.



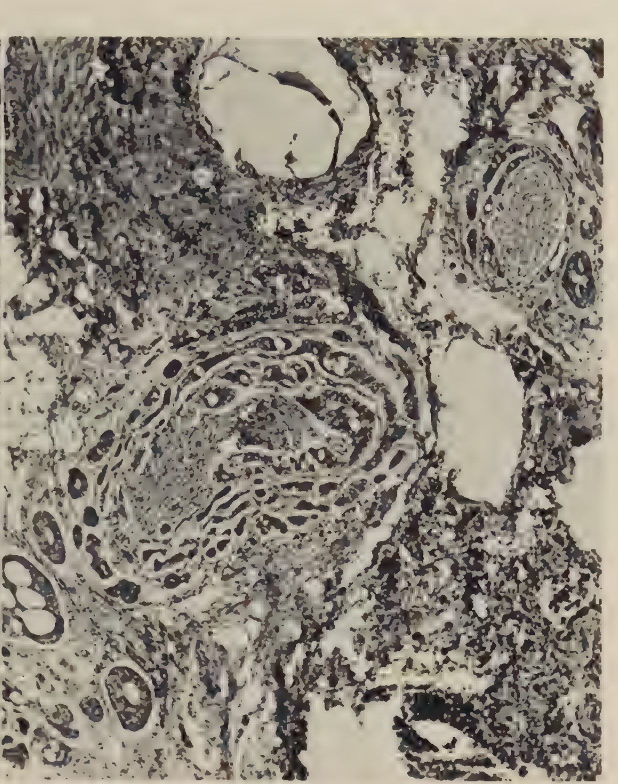
Liver metastases. Primary tumor of right upper lobe bronchus removed by right middle and upper lobectomy ten years after onset of symptoms in 37 year old woman. Liver metastases noted on laparotomy two years later. At death three years after laparotomy, metastasis to brain also reported. Four figures at left from the primary tumor; three at right from liver metastasis. Upper row x 200, lower row x 600.

ADENOID CYSTIC CARCINOMA

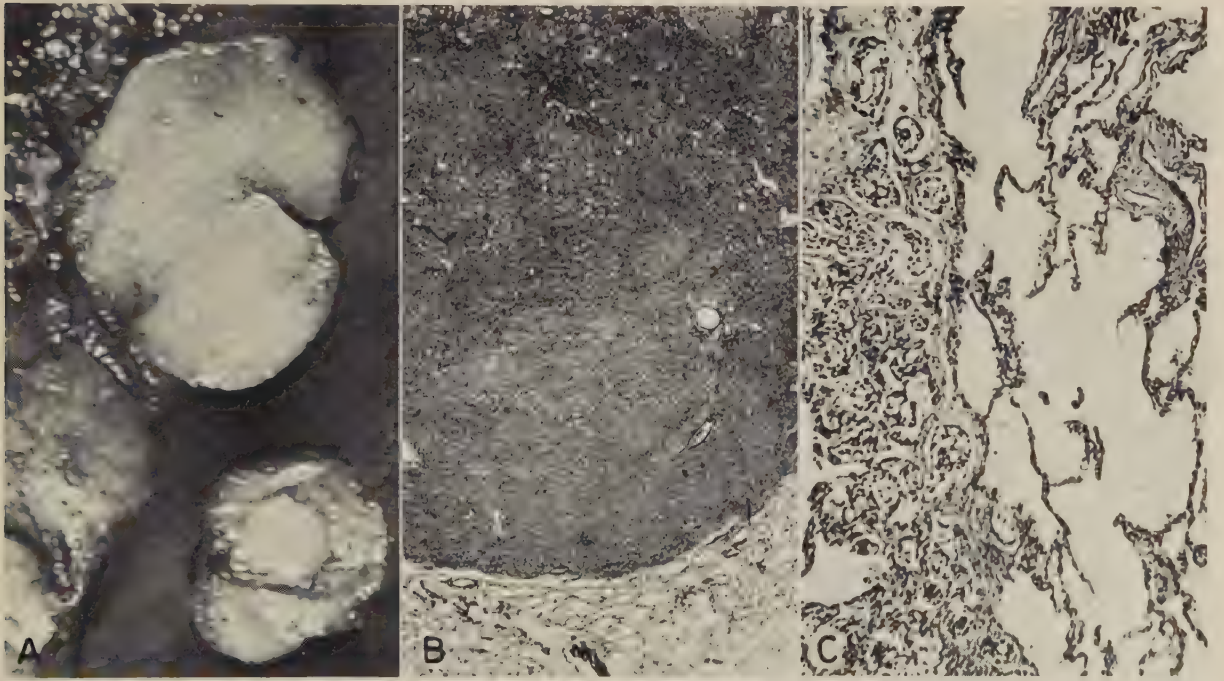
(CYLINDROMA; BRONCHIAL "ADENOMA")



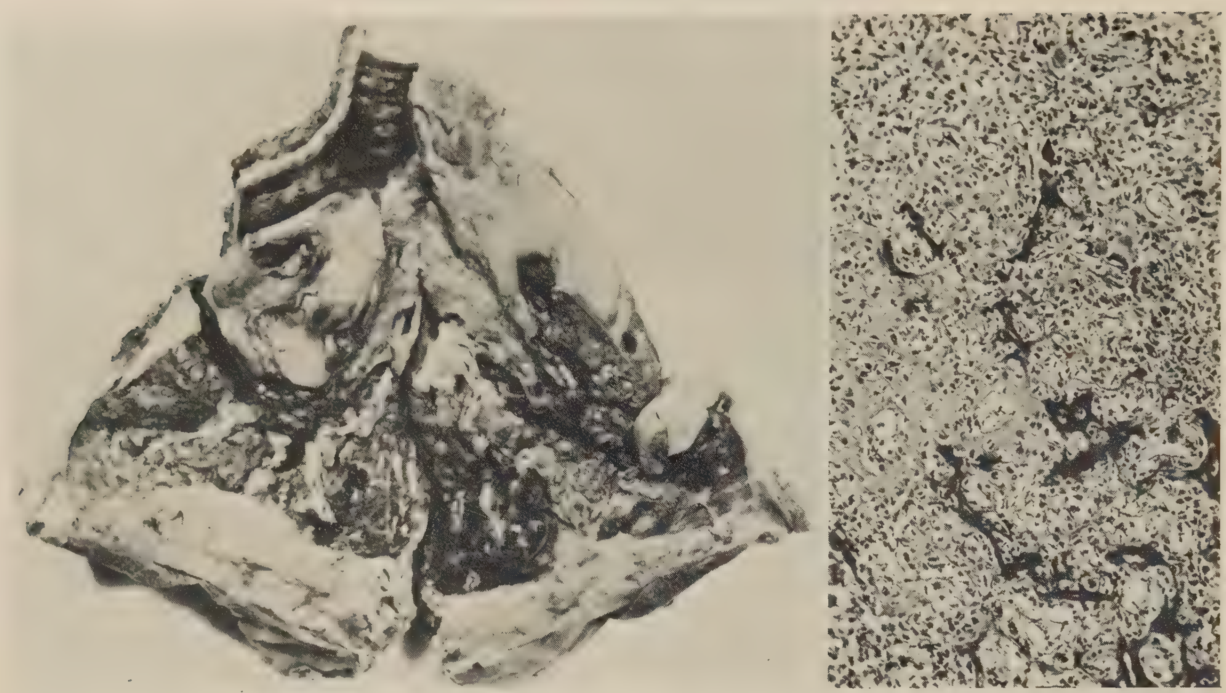
Invasion of bronchial cartilage by large primary adenoid cystic carcinoma of the lung in a 34 year old man. It also widely infiltrated surrounding pulmonary parenchyma. x80.



Perineural lymphatic invasion, extensive, in same case. x48. Despite this frequent and characteristic feature, recurrences and metastases may occur only after many years.

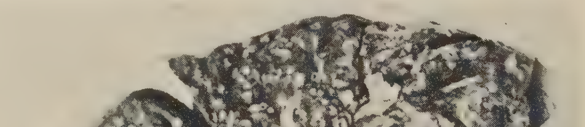


Metastatic adenoid cystic carcinoma in lung. Primary tumor of indefinite origin, presumably pharynx, had been considered incompletely removed ten years previously because it extended into the pterygomaxillary fossa. **A.** Two peripheral metastatic nodules of lung surgically resected. x1½. **B.** Fairly well circumscribed pulmonary metastasis. Histologic pattern identical to primary. x7. **C.** Margin of tumor. Lymphatics in adjacent lung parenchyma also contained tumor. x80. (A.A. Liebow, New Haven, Conn.)

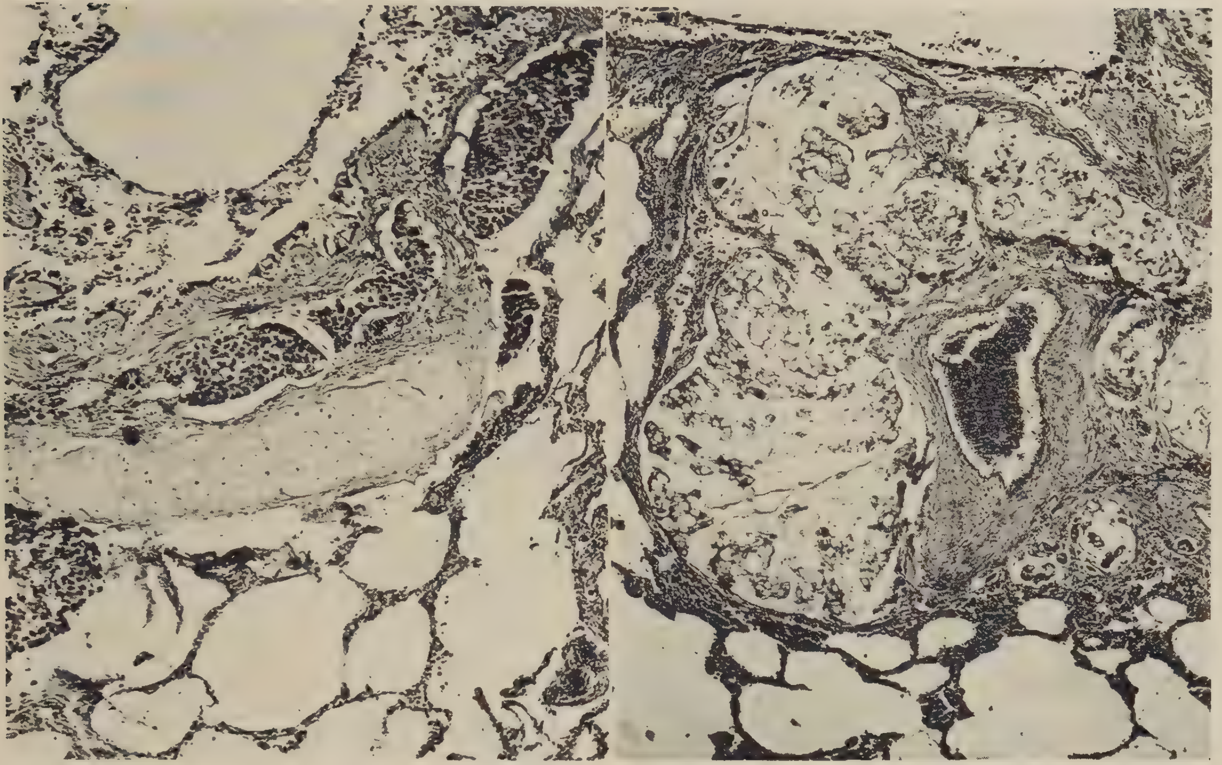


Osteogenic sarcoma, metastatic. *Left:* metastatic tumor in the lung with extension into lumen of right main bronchus of a 43 year old woman; diagnosed by bronchoscopic biopsy. Missing middle finger, presumably the primary site. (P. Holinger and E. Hirsch, Chicago.) *Right:* field showing production of poorly formed bone and osteoid by neoplastic cells, in one of massive pulmonary metastases from a 23 year old man. Primary osteogenic sarcoma of femur removed five months before death. x75.

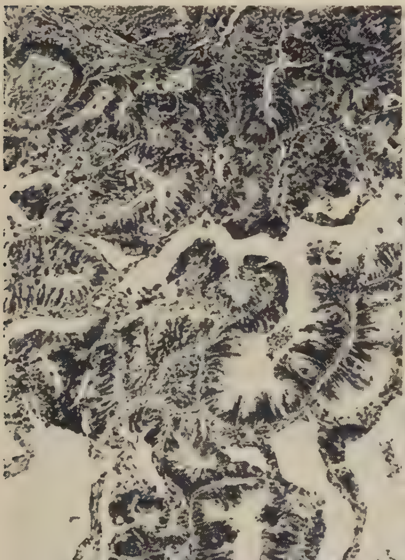
Clear cell carcinoma, metastatic from left kidney of a 62 year old woman. Right lung shows large partially necrotic neoplasm extending into right main stem and lower lobe bronchi and the middle lobe. (E. Hirsch and P. Holinger.)



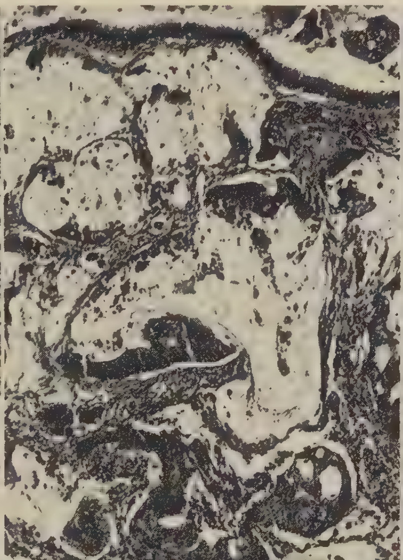
Miliary metastases (blood-borne) from a bronchogenic carcinoma. Small tumor nodules, approximately the same size, were uniformly distributed in the substance of both lungs. Rare case. (E. Hirsch and P. Holinger, Chicago.)



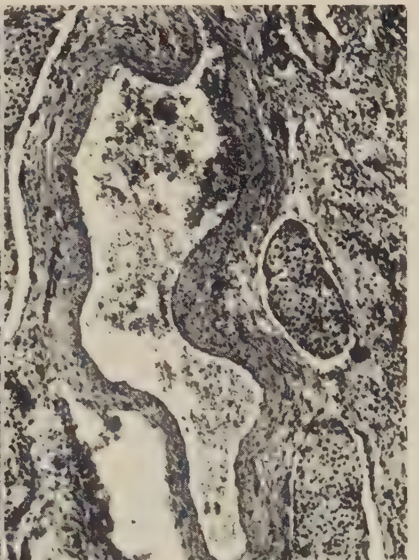
Metastatic adenocarcinoma, primary in stomach of a 30 year old man. *Left:* undifferentiated cell groupings in bronchial lymphatics. x83. *Right:* abundant extracellular mucinous secretion (so-called gelatinous, colloid, or mucoid carcinoma) in metastatic masses within perivascular lymphatics. x62. An example of the lymphangial lung metastases in fulminant gastrointestinal carcinoma, which occurs more commonly in young persons (20-40 years).



Metastatic adenocarcinoma, well differentiated, from primary rectal neoplasm. x83.



Metastatic mucinous adenocarcinoma in lung. Rectum, the primary site. x83.



Metastatic carcinoma in perivascular lymphatics of lung from primary in nasopharynx. x70.

CHAPTER 27

ESOPHAGUS, MEDIASTINUM AND THYMUS

ESOPHAGUS

It is now recognized that **esophagitis** is the cause of a number of symptom complexes. Of the specific acute infections involving the esophagus, diphtheria and scarlet fever are the most important. The superficial fungus diseases, particularly thrush, occasionally extend into the esophagus, especially of infants. Tuberculosis may result from direct infection from infected sputum, or by extension of infection from an adherent tuberculous lymph node. Syphilis of the esophagus, on the other hand, is rare and when it occurs usually is a secondary lesion. Stenosis from syphilis is very rare.

The esophagus shares in the lesions of certain deficiency diseases, most prominently of the acute phases of sprue and pellagra.

Ulcers develop from a variety of causes, usually in the lower end of the esophagus. These can lead to serious hemorrhages or scarring with more or less stenosis. The regurgitation of gastric fluid in debilitated individuals results in digestion of the mucosa.

Occasionally gastric glands are present in the lower end of the esophagus, more rarely in the upper third, and ulcers considered analagous to the peptic ulcer develop in these regions.

The accidental and suicidal swallowing of irritating destructive materials has created serious problems for the bronchoscopist. These substances fall roughly into two classes, the escharotics which destroy by direct chemical erosion and include the inorganic acids and concentrated solutions of heavy metals like arsenic and mercury. These, particularly the acids, may cause early perforation of the esophagus and stomach. Strong alkalies, such as household lye, produce liquefaction necrosis of the mucosa to the point where there may be exfoliation of large portions of it, but the effect is generally not as deep as from the acids. If death is not directly due to shock, subsequent scarring leads to stenosis.

The commonest sites for **stenosis** from any cause are at the levels where the esophagus is naturally constricted; at the cricoid cartilage, at the bifurcation of the trachea, and at the cardiac end of the stomach.

The phenols produce a coagulation form of necrosis in which the tissue is more or less fixed in situ and ulceration is not as prominent a feature. The usual cause of death in such patients is the toxic effect of the phenols, principally on the kidneys. If death does not occur, the coagulated tissue is shed and the subsequent scar formation can also produce stenosis.

For a thorough review of the subject of esophageal stenosis Mosher's writings on the subject should be read.

The most serious circulatory lesion of the esophagus is the **varix,** a complication of interference with portal circulation, classically in atrophic cirrhosis of the liver. Rupture of a varix into the lumen may be the cause of death.

An occasional lesion, usually in infants, is in the form of **cysts** that develop in the lower end of the esophagus. These cysts are of two kinds–a simple retention cyst from the occlusion of a mucus-gland orifice, and the second resulting from an embryonal inclusion of gut epithelium in the deeper layers of the esophagus. Such a cyst is illustrated in the following plates. The patient, a nine-month-old infant, died of inanition. The lesion was discovered at autopsy.

Atresia is the commonest congenital anomaly of the esophagus and usually involves the upper end.

Diverticulum of the esophagus is of two classes: the first resulting from pulsion due to pressue within the lumen on a structural defect in the muscularis. It occurs immediately above the pharyngo-esophageal junction, in fact it is designated the pharyngo-esophageal diverticulum. It is seen predominantly in elderly males. It causes embarrassingly noisy deglutition. It projects to the left posteriorly and may extend into the mediastinum. The opening is usually large enough that food and liquids can easily gain entrance and exit, but if the lumen is small the food gains entrance but is retained, causing destruction by pressure of the subdiverticular esophagus and setting up an intense inflammatory reaction. This form always produces symptoms, the most significant being nocturnal regurgitation. The diverticulum is lined by squamous epithelium but includes none of the muscle layer of the esophagus. In an appropriate specimen it is possible to trace the separation of the normal muscle layers of the esophagus through which the diverticulum has protruded.

The second is the so-called traction diverticulum which is due to the pull on the esophageal wall of a fibrosing inflammatory focus outside of the esophagus. The underlying lesion is usually tuberculosis of a lymph node at the bifurcation of the trachea. It is therefore an anterior defect in contrast to the pulsion diverticulum which is posterior, with the additional differences in location. It is rarely detected during life. Histologically, it is seen that this diverticulum is made up of an extension of the entire wall of the esophagus. Vinson described a variation of this type, the traction-pulsion form that is the consequence of obstruction below a traction diverticulum. This results in an increase of pressure in the original lesion.

Tumors.—Benign tumors of the esophagus are rare, although adenomas, polyps, angiomas, myomas and lipomas have been reported. It is not unusual for a benign tumor to attain considerable size before it produces significant symptoms. When pedunculated it may be regurgitated.

The malignant tumors are predominantly squamous cell carcinomas. Adenocarcinoma occasionally develops and usually at the cardiac end of the esophagus. The epidermoid carcinoma is much more frequent in males than in females and is predominantly a tumor of older persons. CARCINOMA OF THE ESOPHAGUS constitutes 3.5 to 7 per cent of all malignant tumors. Chronic irritation is considered to be a definite etiologic factor, and the high incidence in the tea-drinking nations, the English and Chinese, has been cited as evidence of this. It is rare in the Negro. It is one of the commonest malignant tumors among Chinese males. It is most often found at the sites of natural constriction, especially at the level of the bifurcation of the trachea. It may begin on a basis of leukoplakia, although sometimes the original lesion is more verrucous. Grossly, carcinoma of the esophagus tends to be fungating with considerable ulceration. Less common is the constricting type which infiltrates the loose tissue about the esophagus after undermining and eroding the mucosa. A practical point to remember in biopsy is that the tissue should be obtained from the lower margin of the ulcerated area because the esophagoscope may push uninvolved mucosa over the upper edge of the tumor. Early invasion of the adjacent lymph nodes and the contiguous portion of the trachea may lead to fistula. Microscopically, the tumors are predominantly of the epidermoid type with more or less squamous differentiation including pearl formation.

Post-cricoid carcinoma predominates in women, and in Sweden oropharyngeal carcinoma occurs with equal frequency in men and women. This introduces the subject of the PLUMMER-VINSON SYNDROME. This has been emphasized by Ahlborn as a precursor of carcinoma of the pharynx, mouth and esophagus in women. The syndrome is almost entirely confined to women. It consists of dysphagia and anemia, often accompanied by achlorhydria. At times there is only achlorhydria. The Plummer-Vinson syndrome or the simple achlorhydria is evidently a nutritional disorder. An anemia of the hypochrome type beginning in early life, frequently associated with the early loss of the teeth, dysphagia and achlorhydria are the initial features. It has been found that when patients with this history reach the fourth or fifth decade they show a higher incidence of carcinoma of the mouth and hypopharynx than normal women. Patients that have not shown achlorhydria have also been included in the group. In these patients trophic changes usually are seen in the tissues about the lips and in the mucosa of the mouth and throat, with a dryness that suggests atrophy of the mucosal glands. Spoon-shaped nails are also part of the clinical picture.

The dysphagia is apparently due to organic changes in the pharyngeal and esophageal mucosa. In the radiotherapeutic clinic of the Stockholm Cancer Institute it was found that of 150 women who had squamous cell carcinoma of the mouth, pharynx and esophagus, 70 per cent gave a history indicating the Plummer-Vinson syndrome. Association of the syndrome was especially striking in the cases of post-cricoid carcinoma, a form typically of women.

The suggestion is made that the hypochromic anemia of young females, especially with achlorhydria, be taken seriously, and treatment be instituted as a prophylactic measure against the possible development of mouth and pharyngeal carcinoma.

A comprehensive review of the literature on the surgical management of carcinoma of the esophagus was made recently by Leiter.

SECONDARY CARCINOMA OF THE ESOPHAGUS in most instances is associated with carcinoma primary in the pharynx, larynx, bronchi or stomach and occurs by extension rather than by true metastasis. Gross and Freedman, in reporting a case of obstructing secondary carcinoma of the esophagus from a primary prostatic tumor, reviewed the literature and found 42 acceptable cases. Toreson, in a study of 3700 consecutive autopsies, found 26 instances of secondary tumor of the esophagus. Twenty-four of the metastasizing tumors were carcinomas, one a lymphosarcoma, and one a probable malignant melanoma. The primary tumor was distant in 8 of the 26 cases. Twelve of the tumors caused obstruction, either partial or complete. The total of almost 70 cases collected from the literature or reported in these two articles alone refutes the impression that secondary esophageal carcinoma is very rare.

MEDIASTINUM

Pyogenic infection of the mediastinum is most frequently a complication of an otolaryngic episode. Rupture of the esophagus during esophagoscopy or in passing a stomach tube is a possibility. The vulnerability of the thin wall of the hypopharynx to such an accident has been mentioned, and ulcerations, inflammatory or neoplastic, of the esophagus make the accident possible in the lower portions of the mediastinum.

Extension of infections from the pharynx and neck are no longer as prevalent as before the availability of modern antibiotics. Retropharyngeal and maxillopharyngeal abscesses are now the commonest sources of infection. Early surgical drainage and vigorous antibiotic treatment of the abscesses are essential to avoid the serious and rapidly developing mediastinitis and emphysema otherwise possible.

Neurofibroma, or preferably, **peripheral ganglioneuroma,** is the commonest "free" tumor of the mediastinum. It arises usually from the phrenic nerve and is manifest clinically, therefore, as an alteration in the cardiac shadow. It is benign and attains surprising size without producing symptoms. Histologically, it resembles other peripheral nerve tumors, consisting of interlacing bundles of fibroblastic tissue, palisaded nuclei, varying amounts of collagen, and at times ganglion cells.

The mediastinum is the seat of **cysts** of a variety of origins, chiefly congenital, arising from tracheal, bronchial, esophageal, and gastrointestinal anlagen. Laipply has published a comprehensive review of mediastinal cysts. Cysts of lung, either congenital or the acquired bullous blebs, may impinge on the mediastinum and occasionally rupture into it, resulting in mediastinal emphysema, a painful and disturbing episode, but not necessarily serious.

The abundant lymph nodes in the mediastinum, including the hilar and tracheal nodes, are the seat of chronic granulomatous inflammations–tuberculosis and the systemic mycoses, primary tumors, especially Hodgkin's disease, and secondary tumors, all of which add to the difficulty of interpreting chest roentgenograms.

Teratomas of the mediastinum, according to Schlumberger, arise from the anlage of the thymus. They are rare tumors usually discovered in early adult life, occasionally only as the result of routine roentgenograms of the chest. The presenting symptoms are pain in the chest, cough and dyspnea. Of Schlumberger's sixteen cases, ten proved to be benign both clinically and pathologically, while six were carcinomatous. The malignant element was adenocarcinoma and in four cases there was metastasis.

These tumors occur in the central portion of the anterior mediastinum and appear on x-ray examination as exaggerations of the cardiac shadow and of the hilum of a lung. Pathologically they are true teratomas containing elements which arise from all three germ layers, particularly from the entodermal and mesodermal elements, and bronchial and intestinal organoid structures are common. An unusual instance of pancreatic-tissue inclusion was found. It is this emphasis on the bronchial and intestinal elements that indicates the inclusion of totipotential cells in the anlage of the thymus.

THYMUS

The thymus is important for our purposes because of its relationship to status thymicolymphaticus, a controversial complex. There is a big question as to whether the thymus *per se* plays an active role in this phenomenon, although an enlarged thymus that extends well down behind the sternum has been implicated as a mechanical factor in the death of children, and an enlarged thymus undoubtedly can be a cause of difficulty in breathing in young children.

Status thymicolymphaticus is a complex of early life, consisting of hyperplasia of the lymphatic tissue, generally including the peripheral nodes and especially the elements in the intestinal tract, narrowing of the aorta, tendency to feminine secondary sex characteristics, genital atrophy; and usually hyperplasia of the thymus. This last is not always striking and the gland may even be small. The hyperplasia may involve either cortical (lymphoid) or medullary (epithelial) tissue.

There is no doubt about the existence of such a morphologic complex, but not all accept it as of practical significance and tend to criticize the pathologist and clinician who resort to the diagnosis to explain a sudden death the cause of which is not otherwise obvious. Experience, however, would seem to establish the seriousness of the diathesis. Individuals with these characteristics seem to be lacking in the ability to develop an active immunity to infections or to accommodate to traumas that ordinarily are insignificant. The condition usually disappears in adult life. Death is not due to pressure from the enlarged thymus, although an enlarged thymus from any cause may embarrass respiration.

Histologically, the germinal centers of the lymph nodes show varying degrees of necrosis and fibrosis. In the thymus the epithelial corpuscles are enlarged, degenerated, and cystic. The cysts contain fragments of hyalin and, at times, calcium.

One clinical entity is the **Dubois abscess.** This is not an abscess in the strict sense, but rather a cyst which arises in the remnants of the epithelial duct from which the epithelial elements of the thymus develop. An accumulation of debris may create a clinically evident mass. It was formerly considered evidence of congenital syphilis.

The thymus may be enlarged in hyperthyroidism and there seems to be a definite relationship between a hyperplastic or neoplastic thymus and myasthenia gravis.

There is still mystery surrounding the histogenesis, histology, and function of this gland. While there is no question of the epithelial component forming Hassall's corpuscles, the nature of the small lymphoid cell is controversial. Is it a lymphocyte or a specialized cell, the thymocyte? The tendency now is to consider it the former.

The important tumor of the thymus is the **thymoma,** but it is rare. It is characterized by slow growth, tendency to remain encapsulated, and reluctance to metastasize. Confusing the real incidence of the tumor is the possibility that bronchogenic carcinoma and teratoma may occupy the mediastinal site of the thymus.

It was formerly the custom to divide the thymic tumors into those of the small thymic cell, the true thymoma, and those arising from the epithelial element. It seems now, however, that the thymoma is really a mixture of the two cells in varying proportions and can thus be compared roughly with the lymphoepithelial tumors of the nasopharynx.

Hubbell and Liebow have recently published their intriguing theory that the "epithelial" component is really lymphagiomatous. In their three cases they demonstrate the two elements—lymphocytic and lymphoangiomatous—included vascular spaces and masses of cells they interpret as endothelium. It is true that the vessel-like spaces are a common feature of thymomas.

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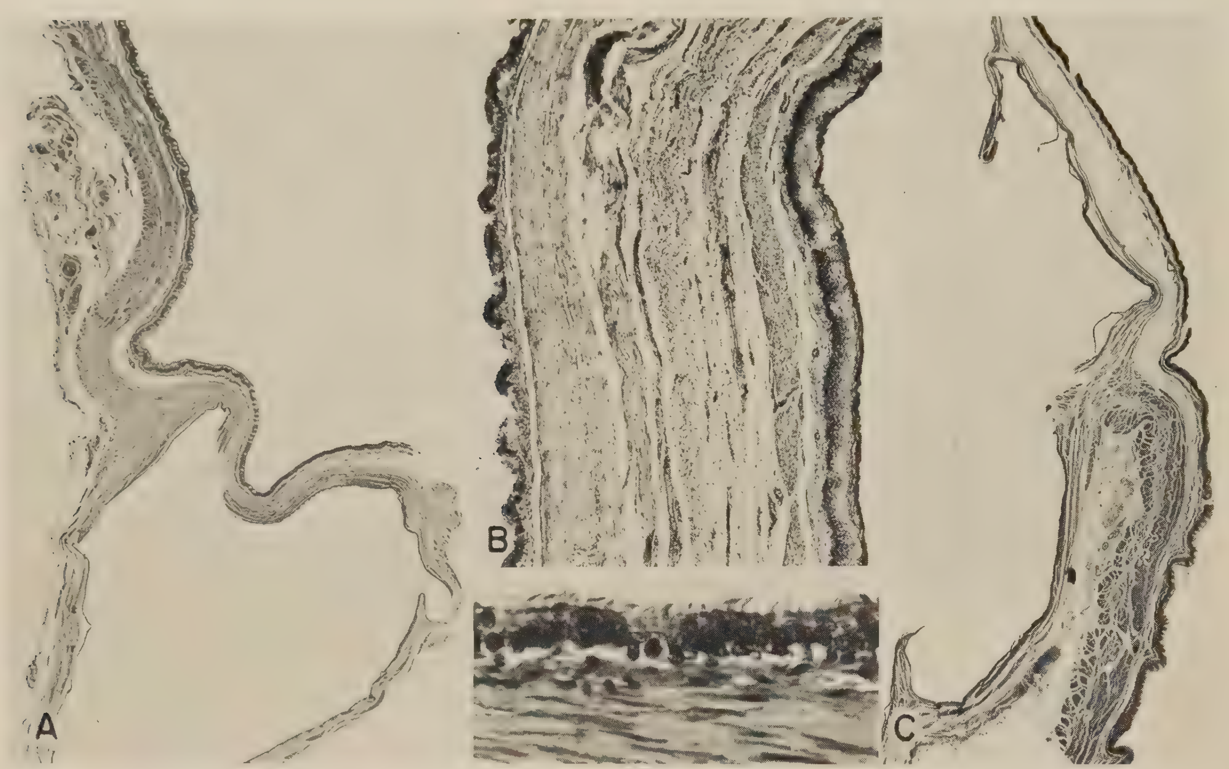
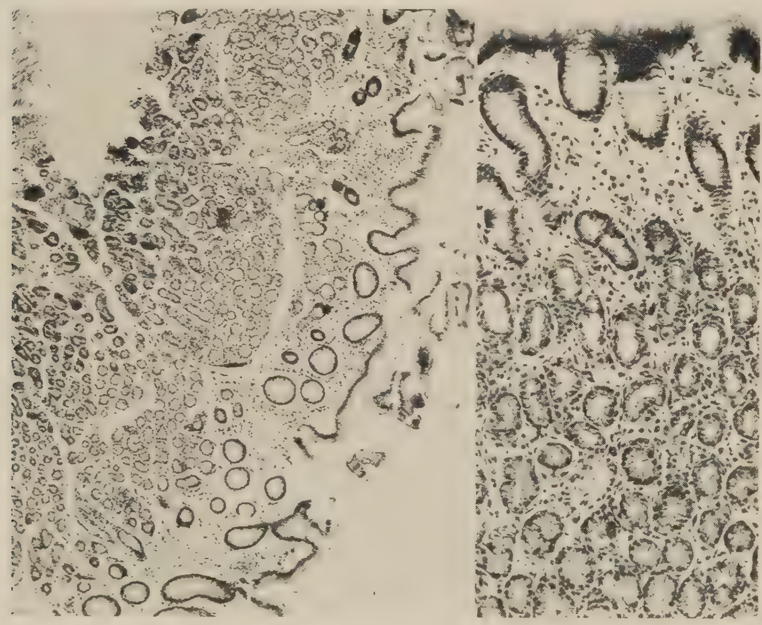
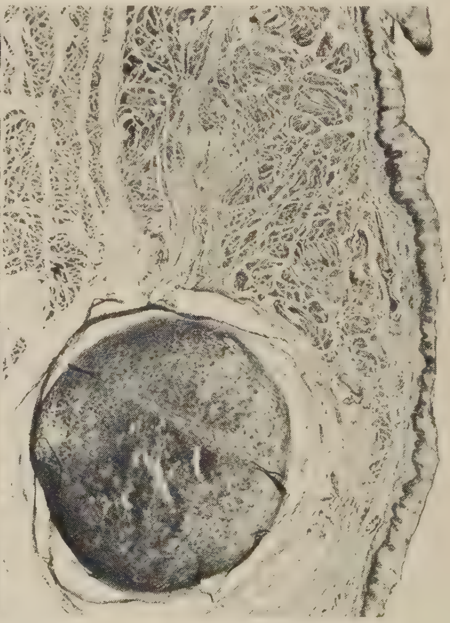
CONGENITAL CYSTS–HETEROTOPIC MUCOSA AND CARTILAGE



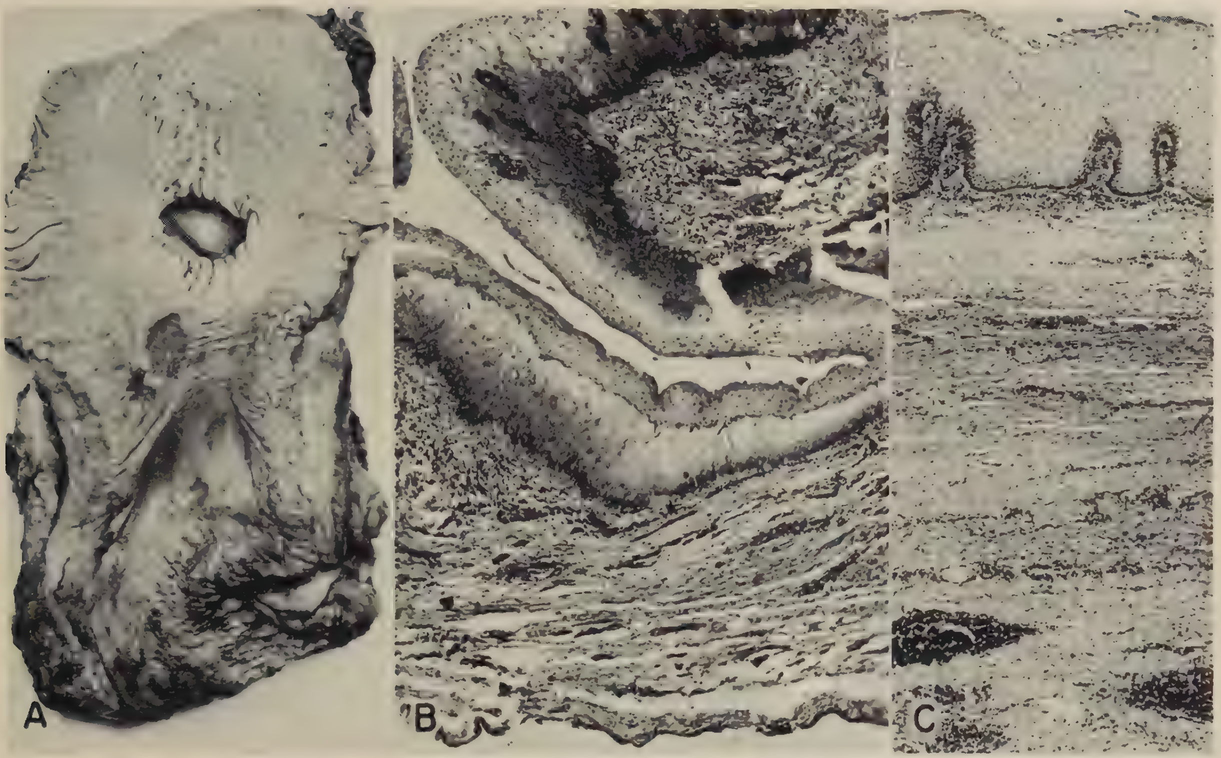
Congenital cysts. A. Large cyst 3 cm. above cardia and within inner muscular coat of esophagus, cause of death in a 9 month old infant. x6. Symptoms of obstruction, including projectile vomiting, at seven months were interpreted as pyloric stenosis. B. Ciliated epithelium lining cyst, at left; stratified squamous epithelium of esophagus, at right; muscularis mucosa, submucosa and part of inner muscle coat between. x48. *Inset:* prominently ciliated pseudostratified epithelium. x395. C. Similar ciliated epithelium-lined cyst, 4 cm. in diameter, from a three year old boy, x6. Such cysts probably arise from misplacement of lung anlage or inclusions of embryonal esophageal tissue, which is lined by ciliated epithelium.



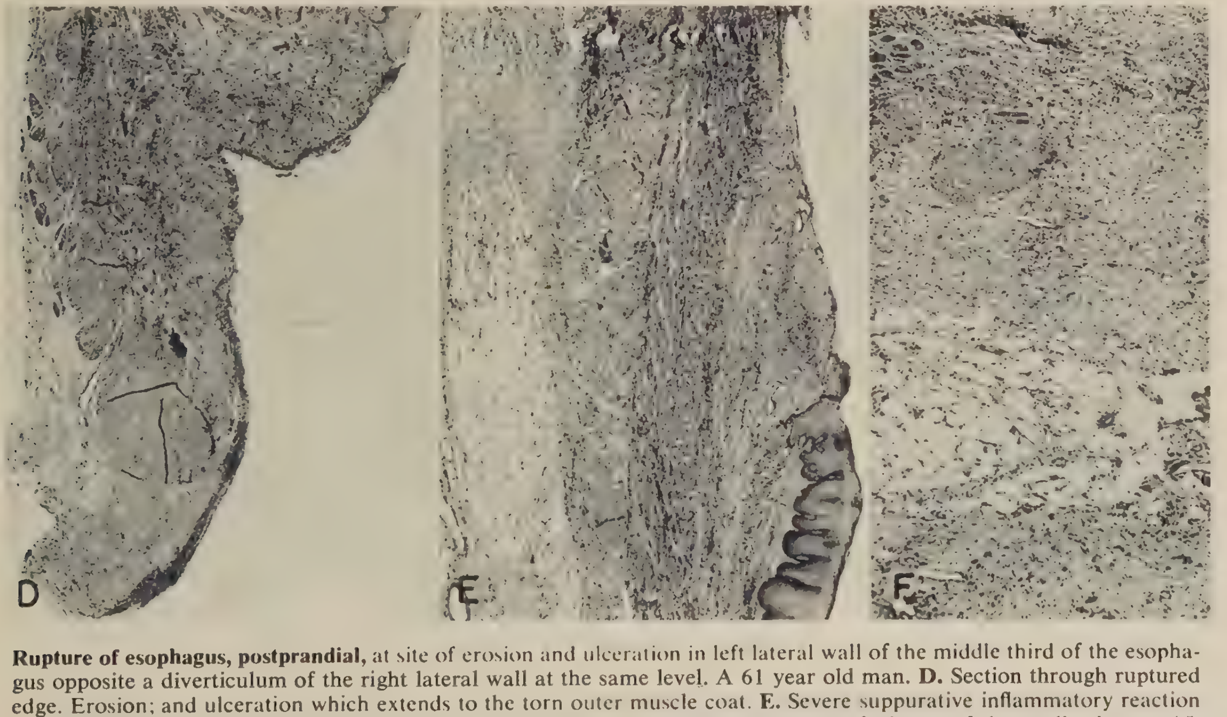
Heteroptopic gastric mucosa. Esophagoscopic specimen from an area 33 cm. beyond incisor teeth of a 32 year old man. Clinical diagnosis of esophageal varices because of episodes of hematemesis for two and a half years. Specimen contains well organized gastric glands. x 48, x 125.



Ectopic cartilage (chorista) within mucularis of esophagus. Nodule of mature cartilage. Incidental finding at autopsy of a 19 year old man. Note also peculiar overdevelopment of muscularis mucosa. x 13.



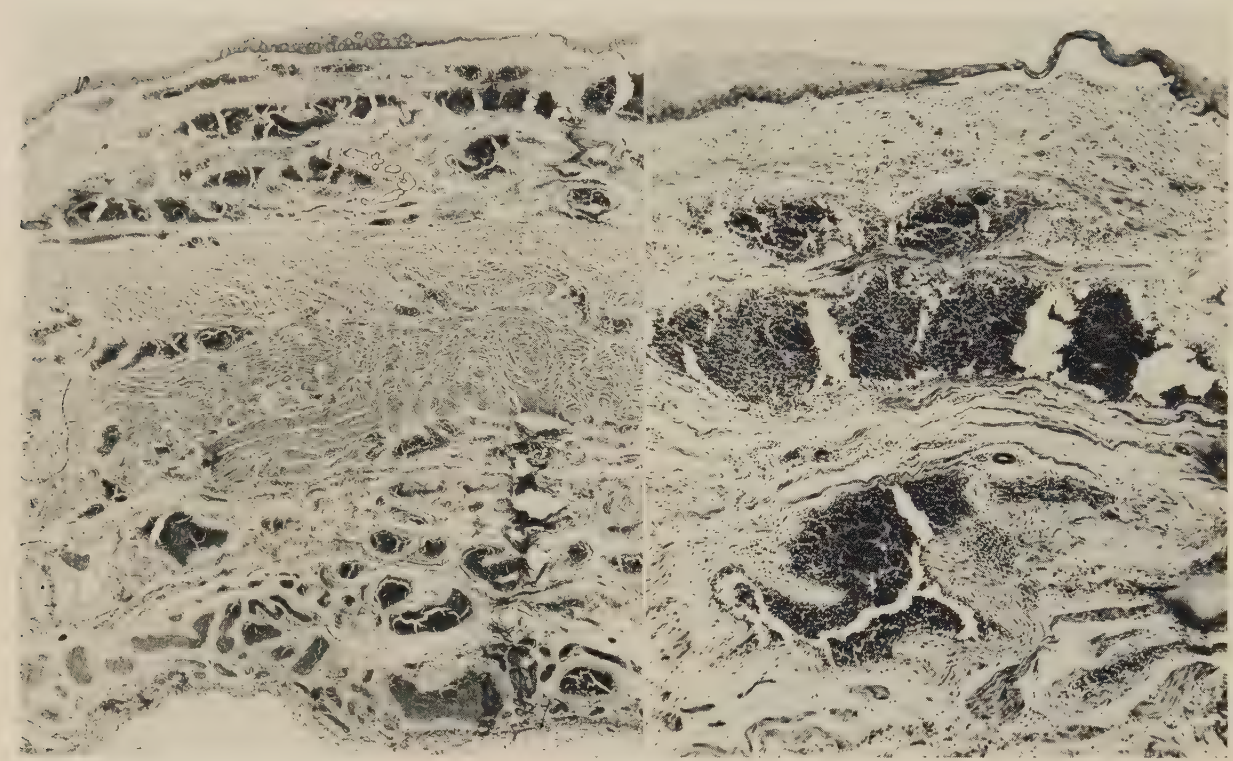
Diverticulum of the esophagus. A. Pulsion diverticulum of Zenker type, on posterior esophageal wall 3 cm. below origin, found at autopsy in 63 year old man with history of regurgitating part of food after each meal and sensation of dysphagia. (P. Holinger, Chicago.) **B** and **C.** Diverticula from elderly men. **B,** removed surgically after two months of dysphagia. Fibrous wall with a few strands of muscle; modified epithelium. x48. **C,** 8 cm. in diameter, with wide mouth, found at autopsy 3 cm. above cardia. Very thick fibrous wall; chronic inflammatory exudate; focal hemorrhages. x48.



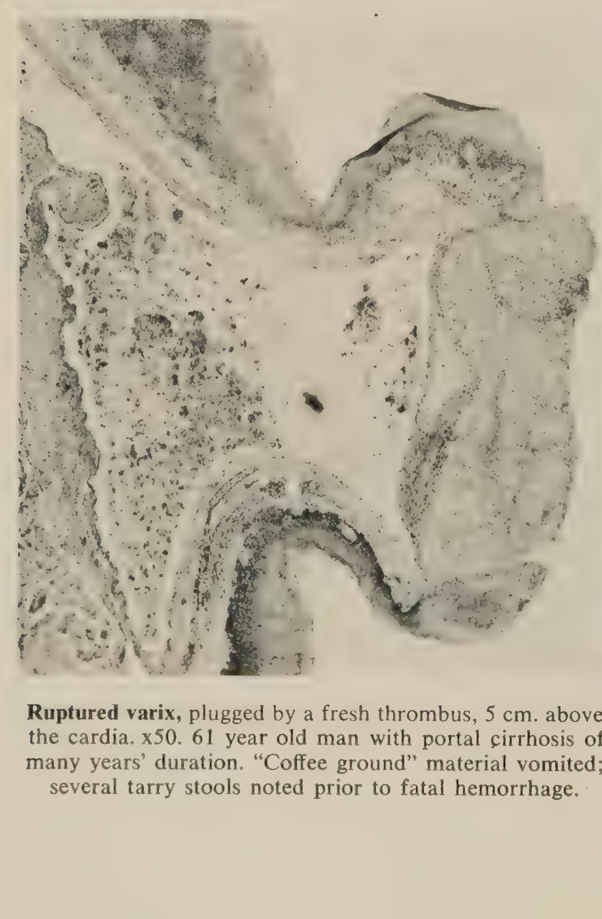
Rupture of esophagus, postprandial, at site of erosion and ulceration in left lateral wall of the middle third of the esophagus opposite a diverticulum of the right lateral wall at the same level. A 61 year old man. **D.** Section through ruptured edge. Erosion; and ulceration which extends to the torn outer muscle coat. **E.** Severe suppurative inflammatory reaction in partly necrotic esophageal wall adjacent to the perforation has extended to the soft tissues of the mediastinum. x15.

F. Acute purulent mediastinitis. Necrotic torn muscle bundles of outer muscle coat of the esophagus at top. x48.

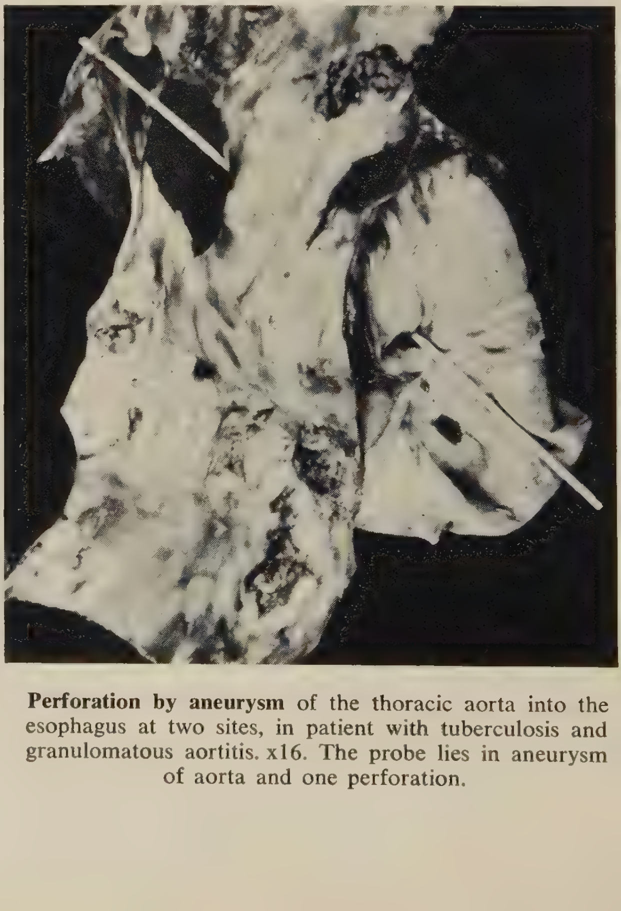
ESOPHAGEAL VARICES
PERFORATION DUE TO EXTRINSIC LESION



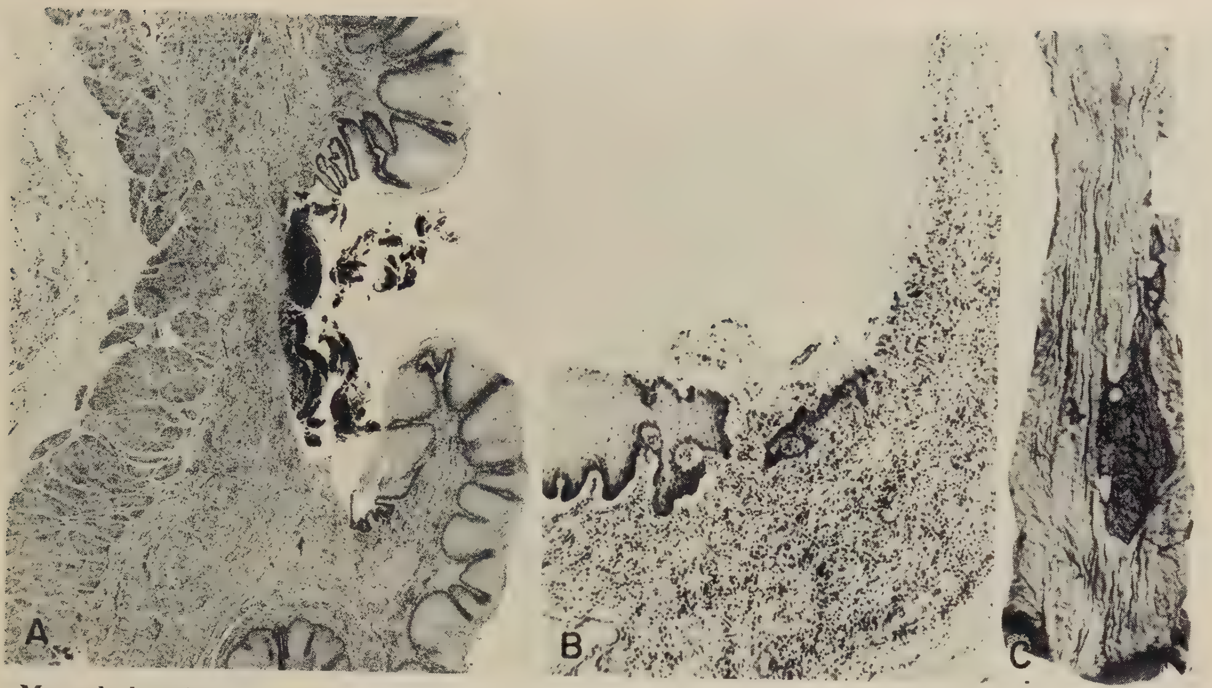
Esophageal varices in a 41 year old Negro man with cirrhosis of the liver. *Left:* entire thickness of esophageal wall with dilated congested veins, rarely so well demonstrated, in all coats; particularly prominent in submucosal and adventitial layers. x12. *Right:* dilated engorged thin-walled veins between fibers of the muscularis mucosa, at higher magnification. Note pronounced mucosal edema and atrophic epithelium over the large superficial varix. x48.



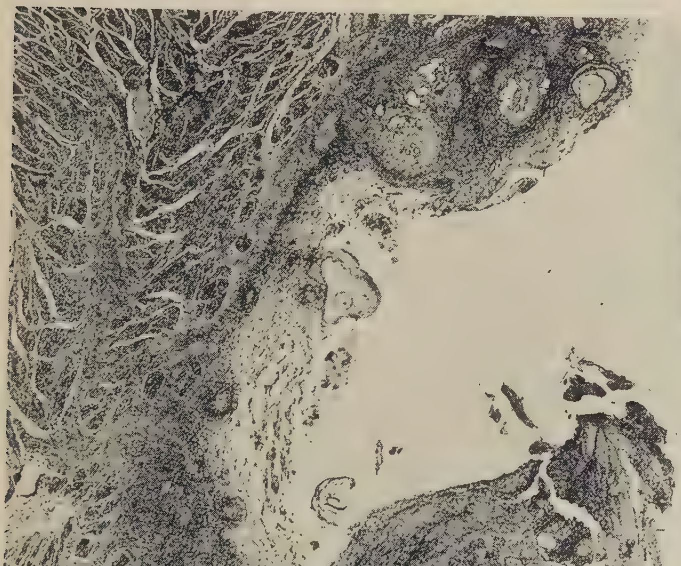
Ruptured varix, plugged by a fresh thrombus, 5 cm. above the cardia. x50. 61 year old man with portal cirrhosis of many years' duration. "Coffee ground" material vomited; several tarry stools noted prior to fatal hemorrhage.



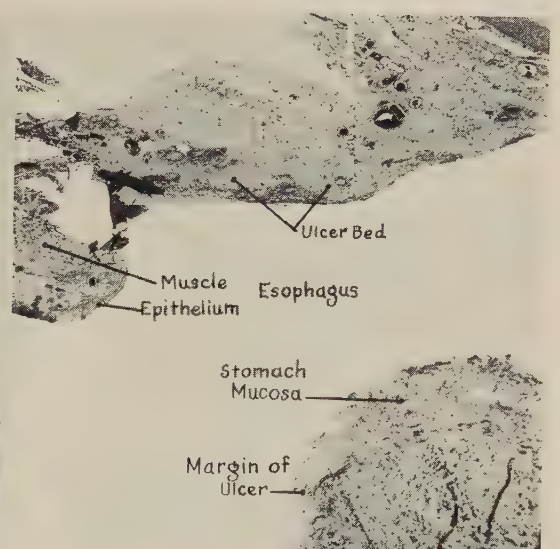
Perforation by aneurysm of the thoracic aorta into the esophagus at two sites, in patient with tuberculosis and granulomatous aortitis. x16. The probe lies in aneurysm of aorta and one perforation.



Mucosal ulcerations. A. Ulceration of proximal esophagus in patient with pharyngeal carcinoma. Dysphagia from extrinsic pressure on esophagus by regional extension necessitated feeding by tube. x13. **B.** Erosion of esophagus with acute and chronic mucosal inflammation in case of virus hepatitis. x40. **C.** Ulcer, presumably resulting from presence of Wangensteen suction tube in esophagus for six days, in patient who died of intestinal obstruction. No previous esophageal symptoms. (P. Holinger and E. Hirsch, Chicago.)



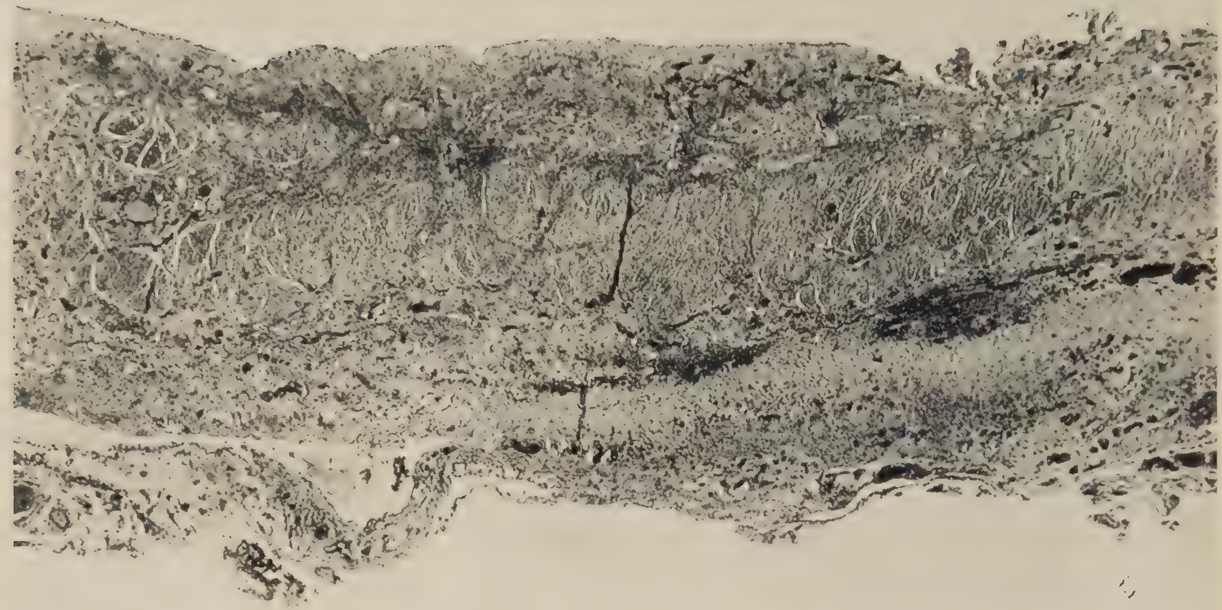
Ulcer extending into muscle coat, one of several in distal third of esophagus in 30 year old man after Bataan Death March. Severe gastrointestinal symptoms with hematemesis for one week and terminal exsanguination. x16.



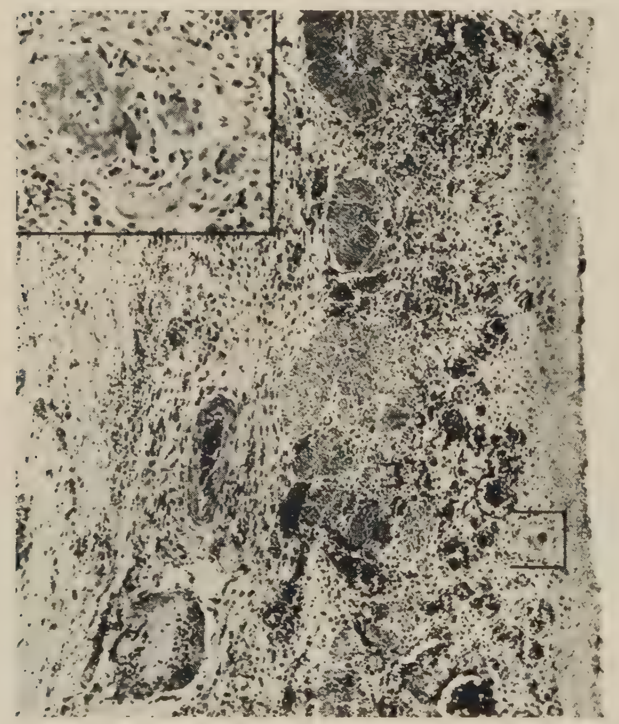
Perforation due to ulcer at gastroesophageal junction. Esophageal margin, *upper*. x5. Gastric edge, *lower*. x10. Death twelve days later with extensive mediastinitis and bilateral pleural empyema.

CHEMICAL INJURY, ESOPHAGUS

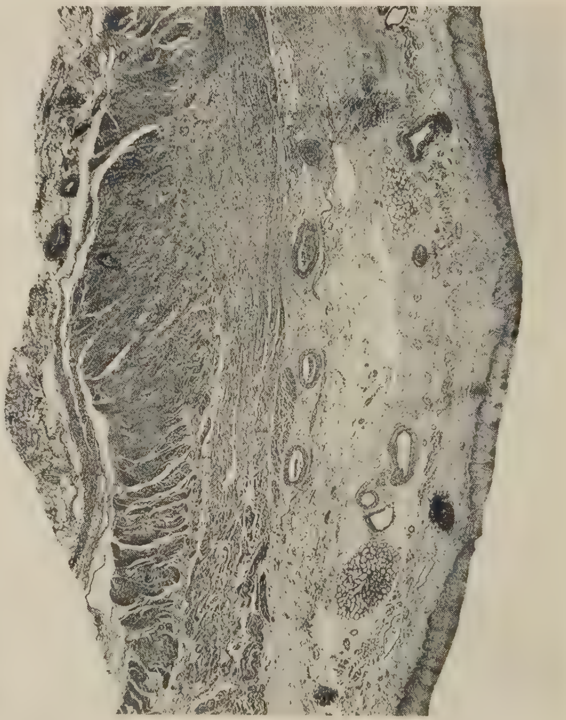
ESOPHAGITIS DUE TO CORROSIVE AGENTS



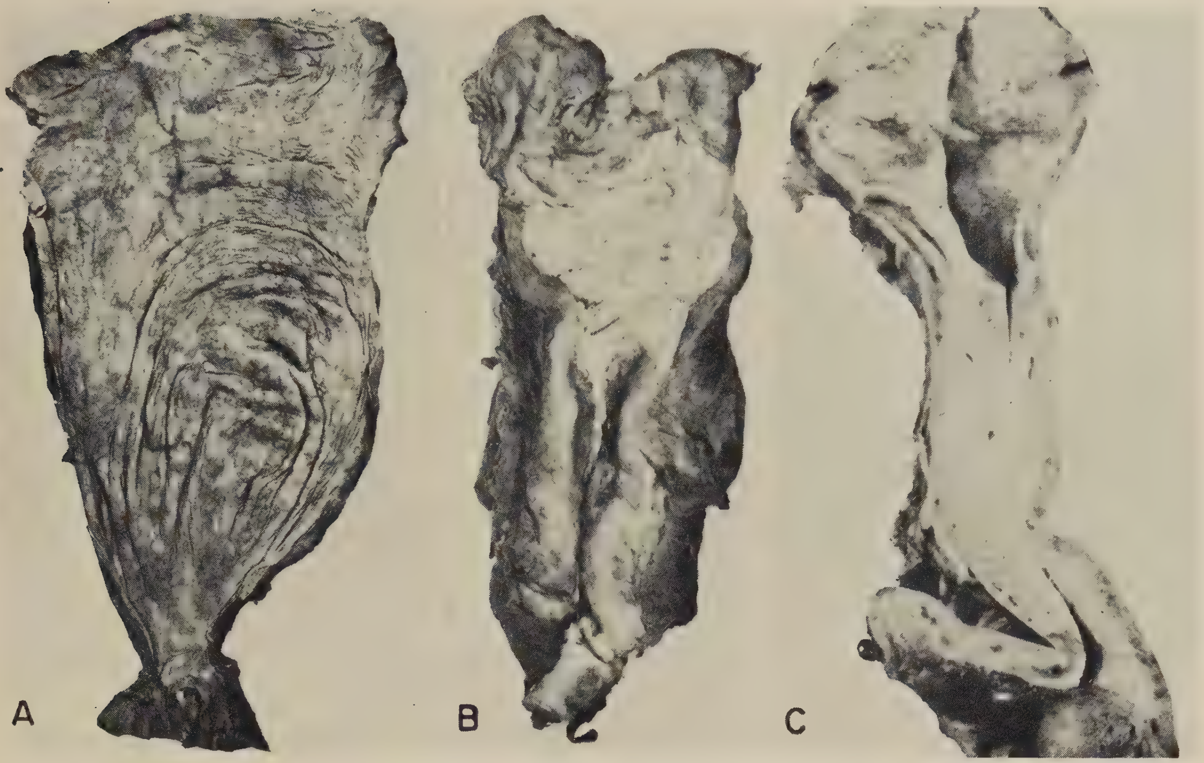
Esophagus after lye ingestion. Unknown quantity swallowed by 36 year old woman, with immediate severe shock. Obvious burns about face, mouth and pharynx. Treated with gastric lavage, eggs, magnesium sulfate and vinegar, but vomiting was continuous and after a time included shreds of tissue. Death on sixth day with laryngeal and pulmonary edema. Large portions of necrotic mucosa and submucosa have been sloughed. Edematous thickening of muscle and adventitial coats with vascular congestion and hemorrhage. x15.



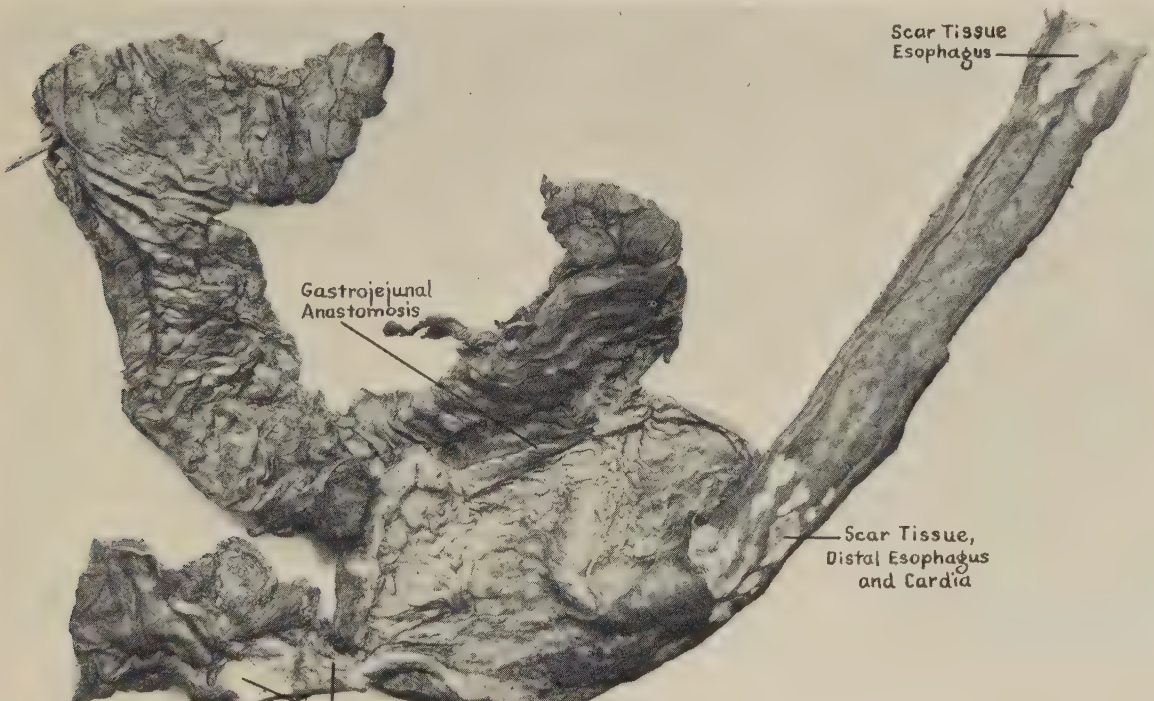
Higher magnification of case above. Partially necrotic exposed muscle layer, marked edema, vascular congestion with interstitial hemorrhages, extensive leukocytic infiltration. x50. *Inset:* magnified view of necrotic, thrombosed artery within blocked area. x240.



Esophagus in acute phenol poisoning, 80 year old man. Architecture "fixed" by coagulation necrosis. Edema and thrombosis, but no ulceration or sloughing. x10. Death presumably respiratory with edema and hemorrhage of larynx and trachea.



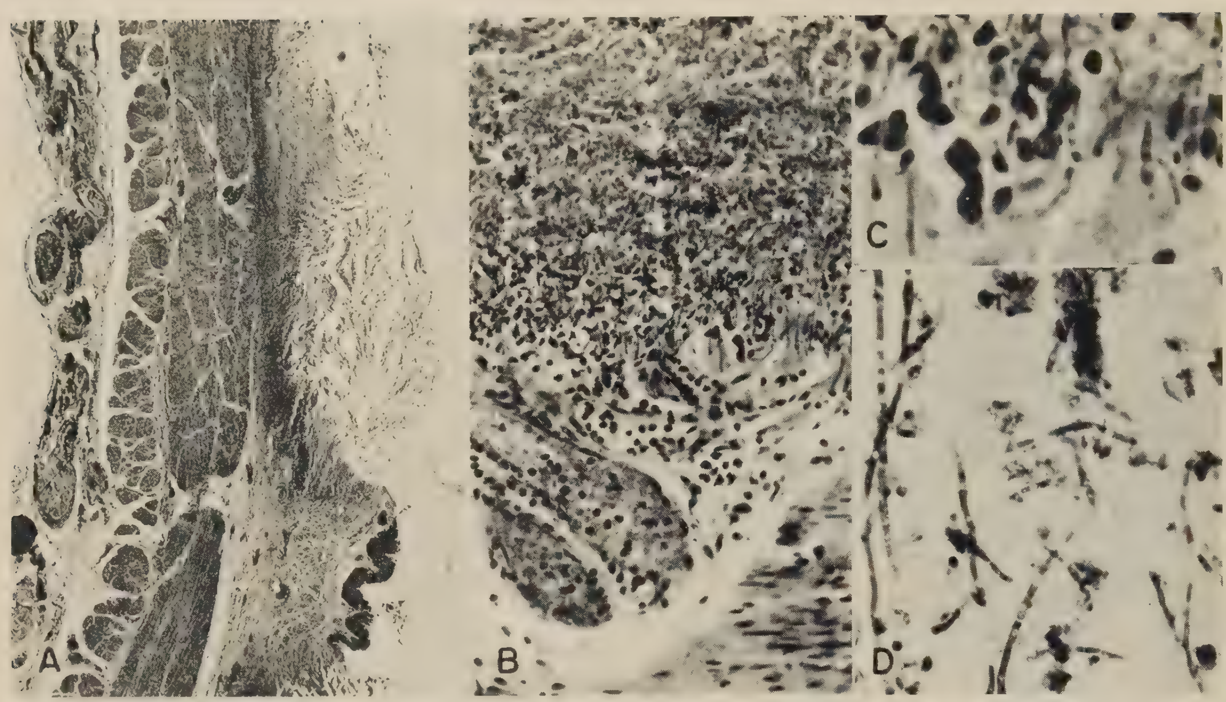
A. Cardiospasm and fibrosis of cardia in 68 year old man, dysphagia five years. **B.** Extensive scarring in 15 year old girl who ingested **lye** at 14 months of age.. **C.** Stenosis of lower third, one year after suicidal attempt with **hydrochloric acid.** Marked hypertrophy and dilatation of esophagus proximal to stricture in each case. (**A** and **B,** P. Holinger and E. Hirsch, Chicago, **C,** University of Göttingen, courtesy of W. Putschar.)


Scar Tissue Esophagus
Gastrojejunal Anastomosis
Scar Tissue, Distal Esophagus and Cardia
Scar Tissue Occlusion of Pylorus

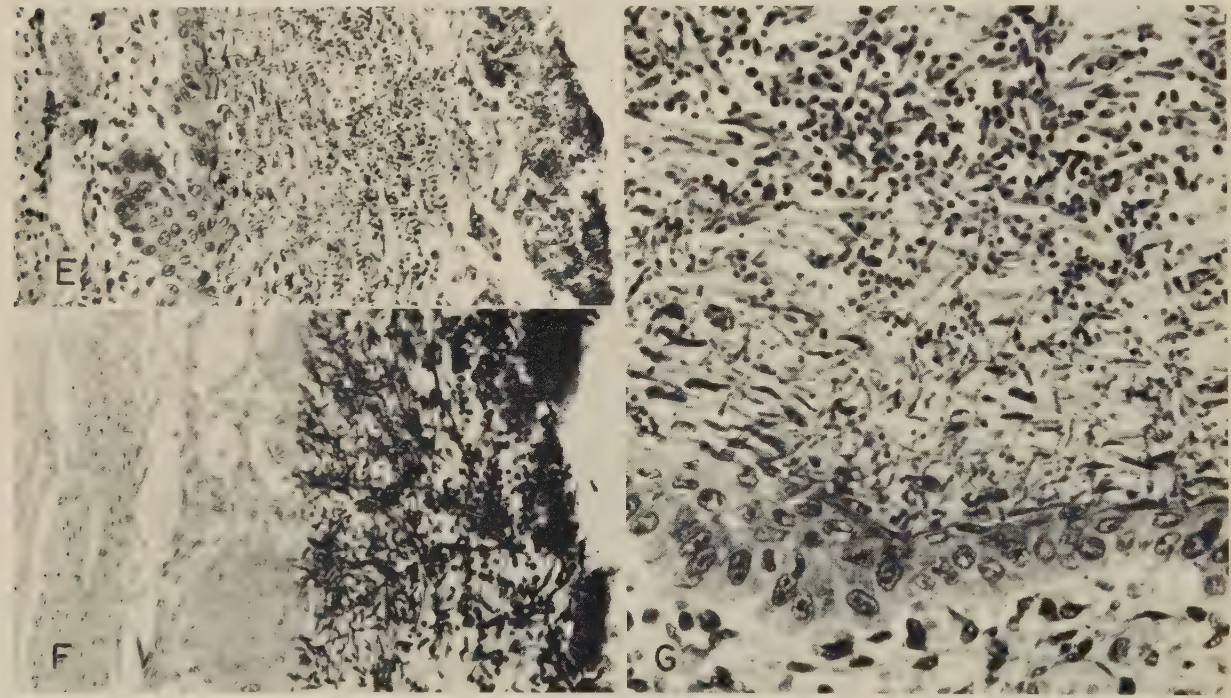
Cicatricial strictures of esophagus and stomach in 57 year old man, seven months after accidental ingestion of hydrochloric acid. Esophageal strictures were dilated and gastrojejunostomy done. (P. Holinger and E. Hirsch.)

CANDIDIASIS, ESOPHAGUS

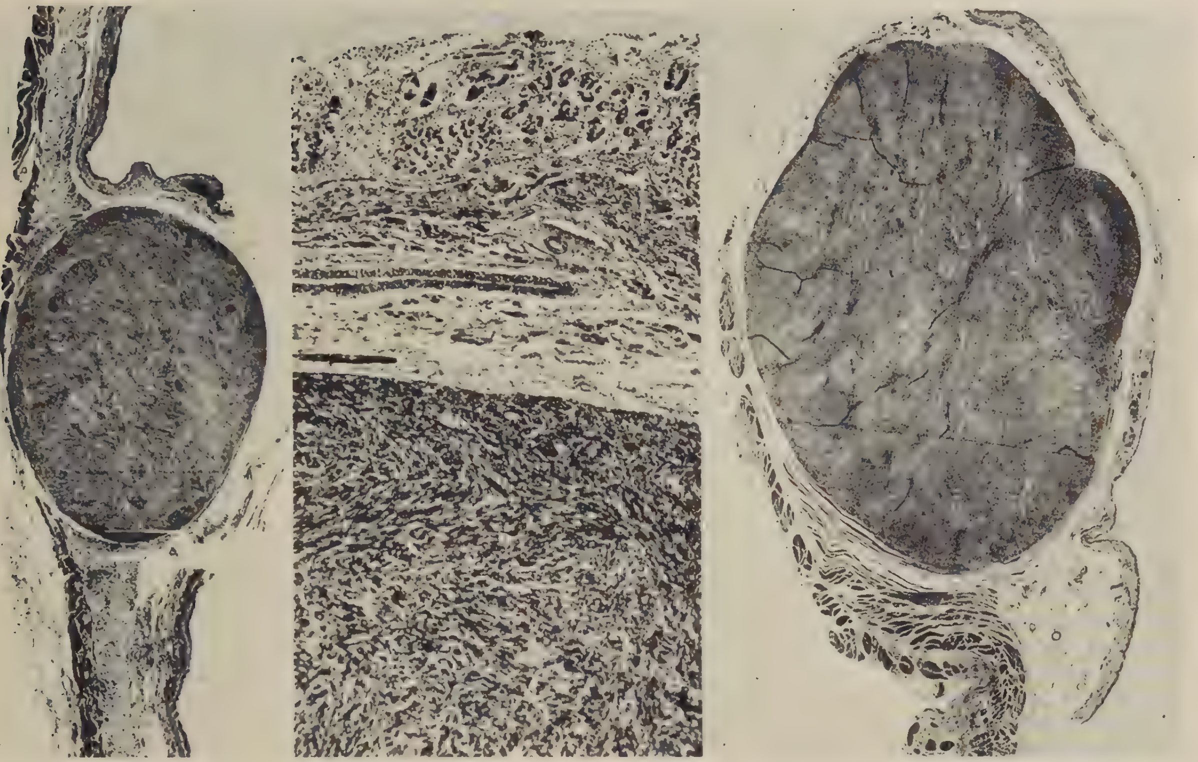
(MONILIASIS; THRUSH)



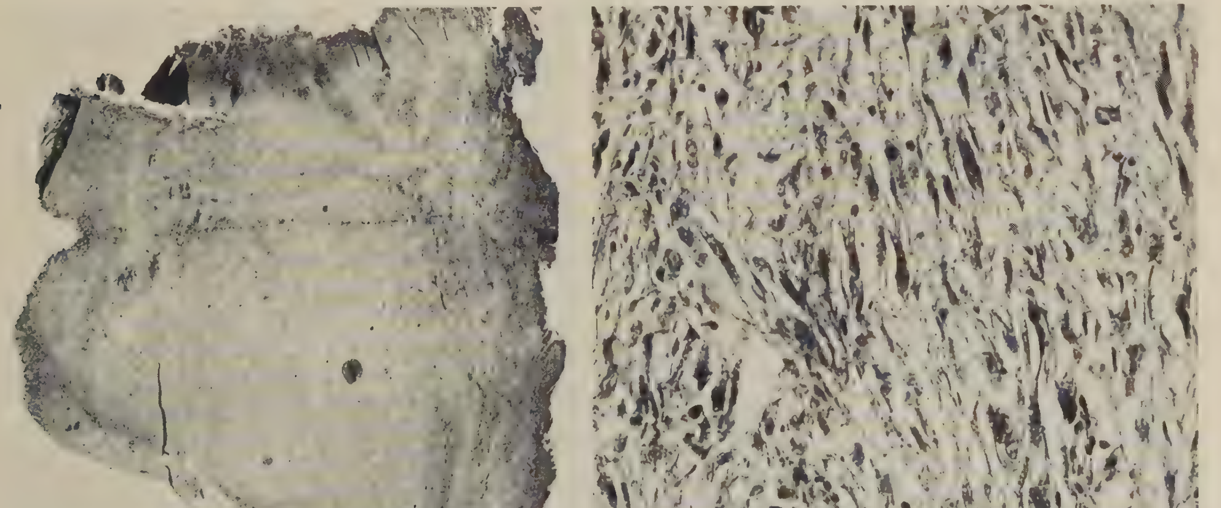
Destruction of mucosa and submucosa to muscle coat of esophagus in a 6 week old infant who died of malnutrition and pneumonia. Oral mucosa also involved. **A.** Practically entire esophageal mucosa macerated and covered with shaggy, adherent, grayish white pseudomembrane. x24. **B.** Membrane on surface of muscle coat composed of tangled hyphae and spores of *Candida (Monilia) albicans,* some of which extend into vessel at center. x210. **C** and **D.** Details of hyphae and spores. x655, x875.



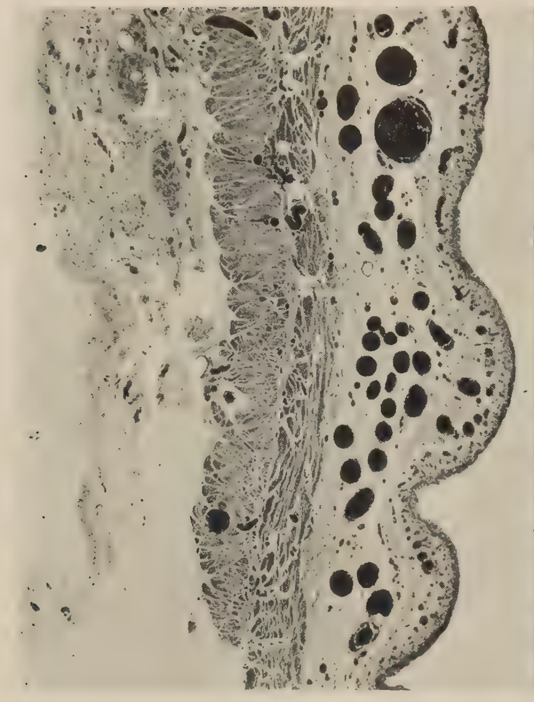
Superficial, less extensive involvement is more common. Candidiasis in 10 week old baby with congenital absence of common bile duct. Mouth, pharynx and upper third of esophagus contained adherent patches of yellow-green material, removed with difficulty. **E.** Hematoxylin and eosin stain. **F.** Bauer stain demonstrates more clearly tangled hyphae and spores, which take brilliant red stain. Both x25. **G.** Epithelium destroyed to basal layer by fungus. No cellular reaction or exudate. x400.



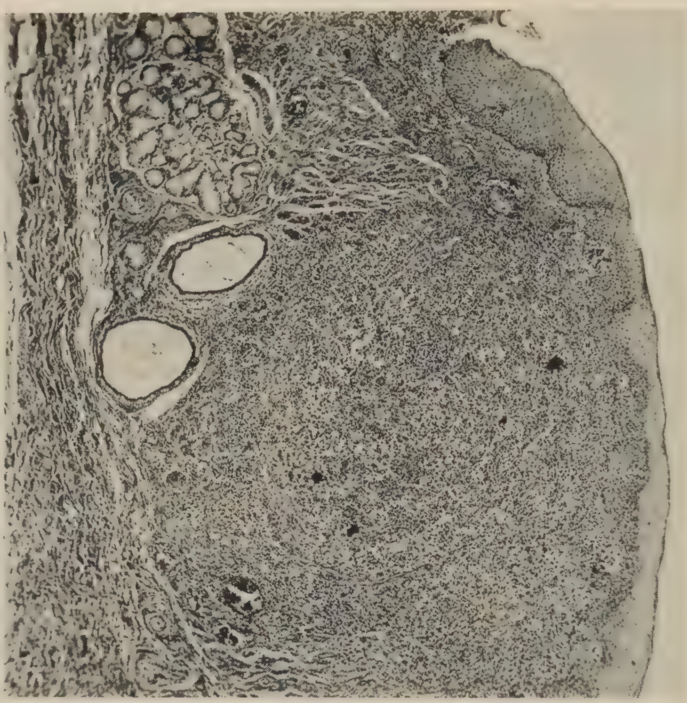
Leiomyoma of esophagus. *Left:* small circumscribed tumor with obvious origin from inner muscle coat. *Center:* tumor at cardioesophageal junction. Gastric mucosa at top. Interlacing bundles of smooth muscle are red, collagen yellow, with Mollier trichrome stain. x45. *Right:* cellular leiomyoma 2.5x2x1.5 cm., in anterior wall of upper esophagus. An incidental autopsy finding in a 61 year old man. x5.



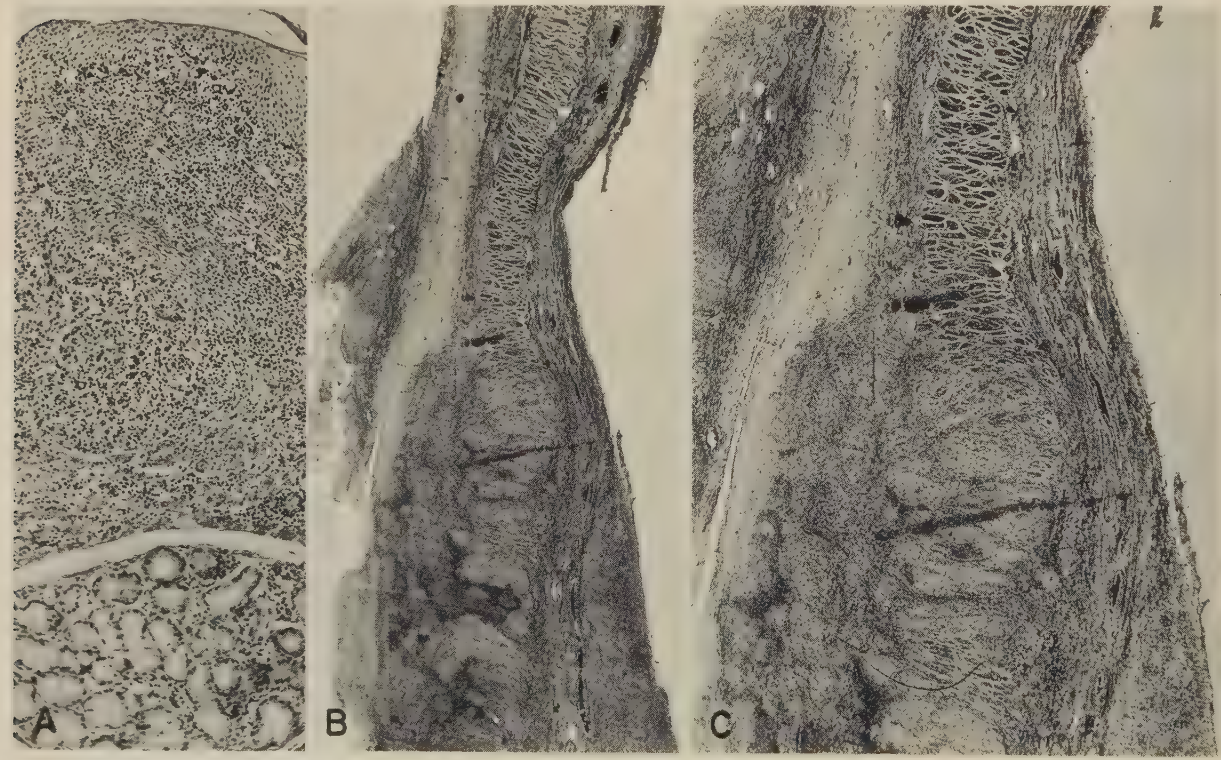
Leiomyosarcoma of esophagus of 32 year old man, which spread to mediastinal structures, lungs, and pleura. *Left:* low magnification of proximal portion of mass infiltrating all coats of esophagus below. It completely occluded the lumen and extended to periesophageal tissues. x5. Typical microscopic field. Pleomorphic spindle-shaped cells with hyperchromatic, frequently bizarre nuclei and numerous mitoses. x235.



Chronic myelogenous leukemia, in a 30 year old white man whose terminal leukocyte count was 592,000. Striking engorgement of vessels with leukemic cells, most prominent in submucosa. x8.



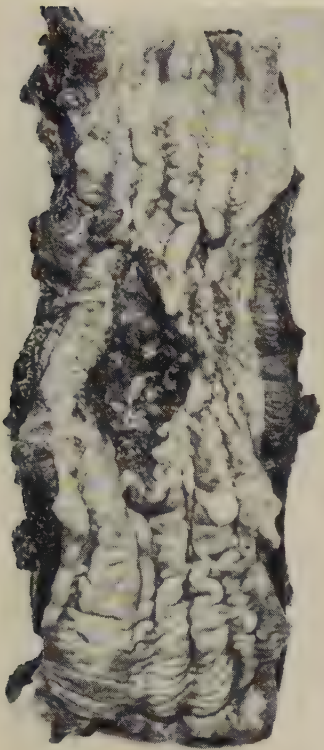
Hodgkin's disease. Diffuse polymorphous cellular infiltration, characteristic of the disease, has appreciably widened mucosa and submucosa. Epithelium intact. Mucosa of pharynx and trachea similarly involved. x48.



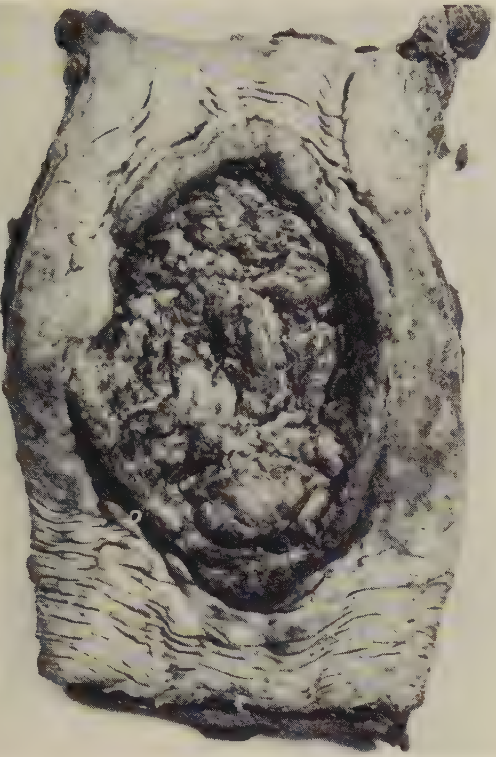
A. Large cells (Reed-Sternberg) are numerous in this field, from case above. x70. **B** and **C.** Esophageal involvement in sarcomatous Hodgkin's disease, apparently by direct extension from mediastinal mass to periesophageal tissues. Extensive neoplastic infiltration of all coats of esophagus, gradually obliterating architecture of organ (at bottom). The lungs and trachea were also secondarily involved. x8, x12. 33 year old man with asthenia; fever; progressive enlargement of lymph nodes; death three years after onset.

CARCINOMA OF THE ESOPHAGUS

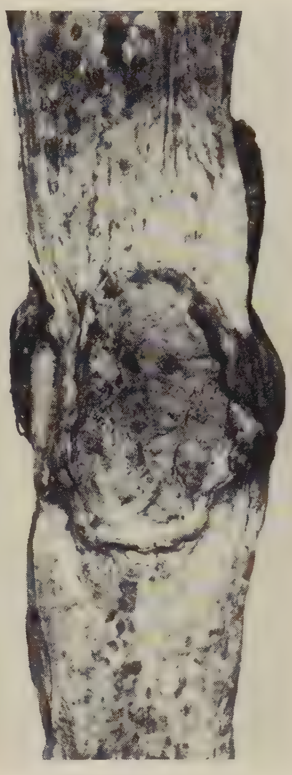
SURGICAL SPECIMENS



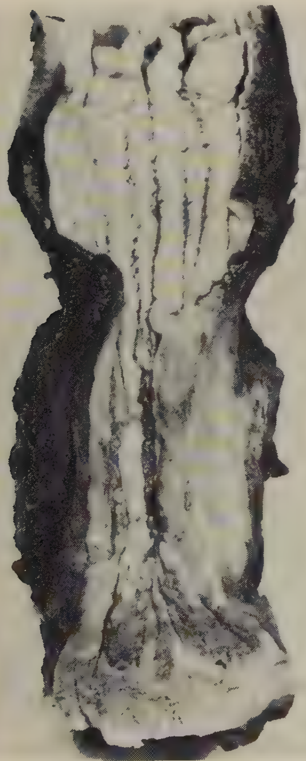
Ulcerative carcinoma, midthoracic esophagus. 62 year old man.



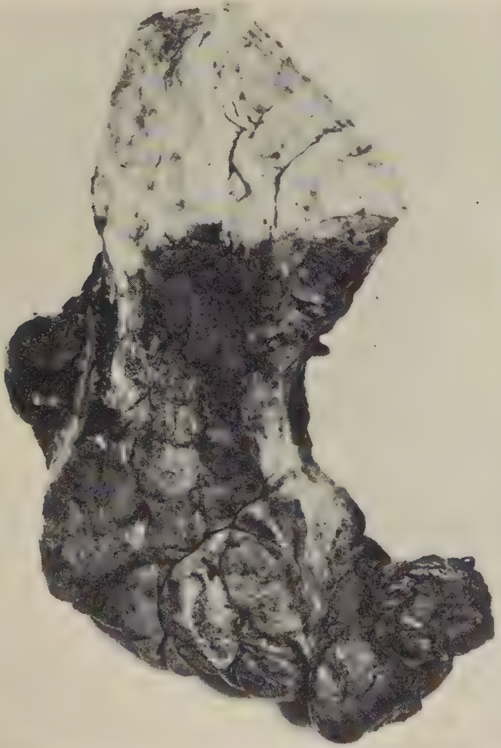
Exophytic, fungating carcinoma. Lower segment of esophagus of an elderly man.



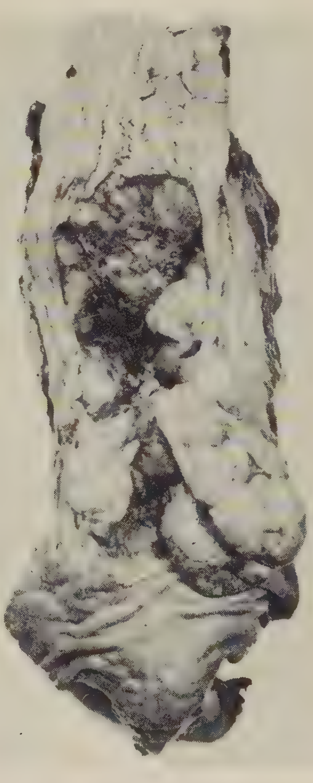
Annular carcinoma, that metastasized. 65 year old man.



Annular, infiltrating carcinoma, distal segment. 51 year old man.

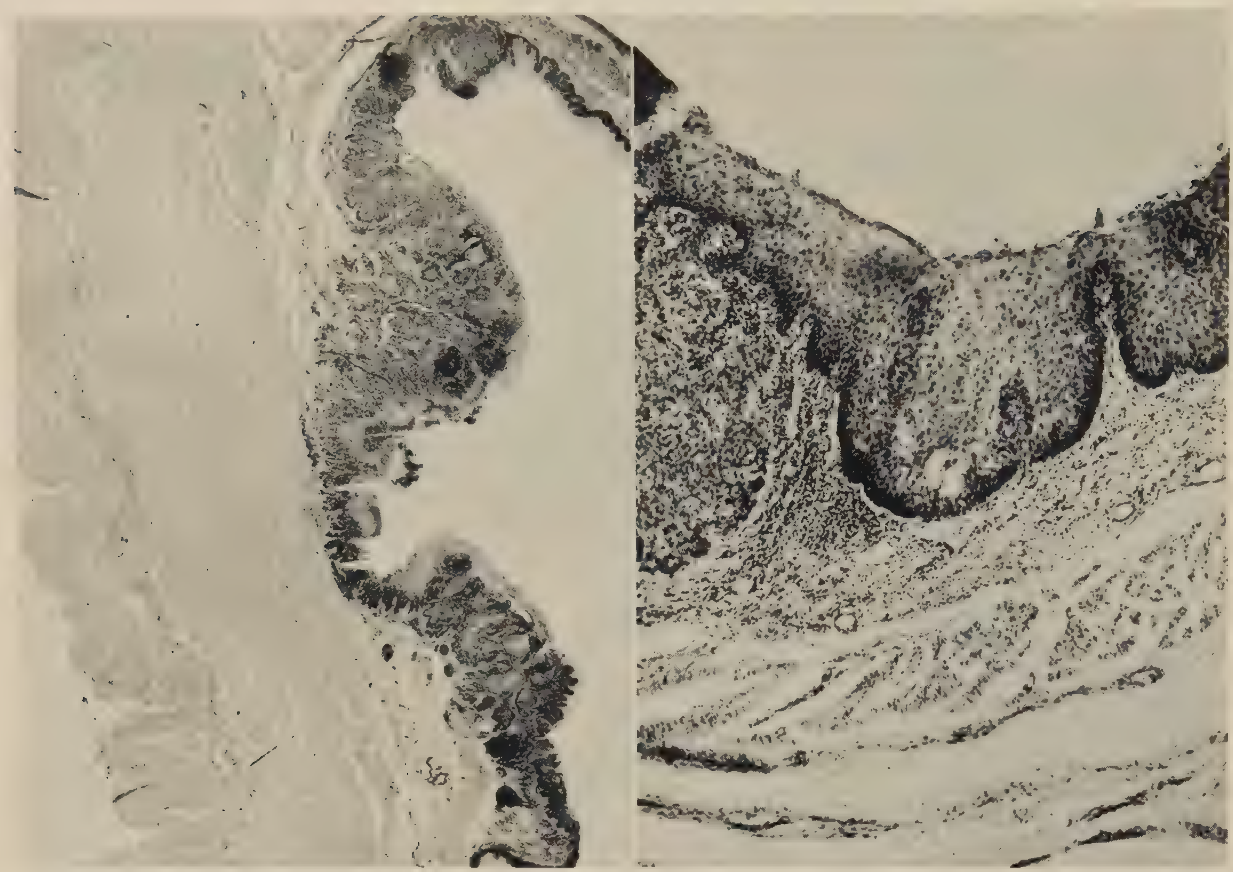


Adenocarcinoma, cardioesophageal junction, infiltrating esophageal wall above and stomach below.

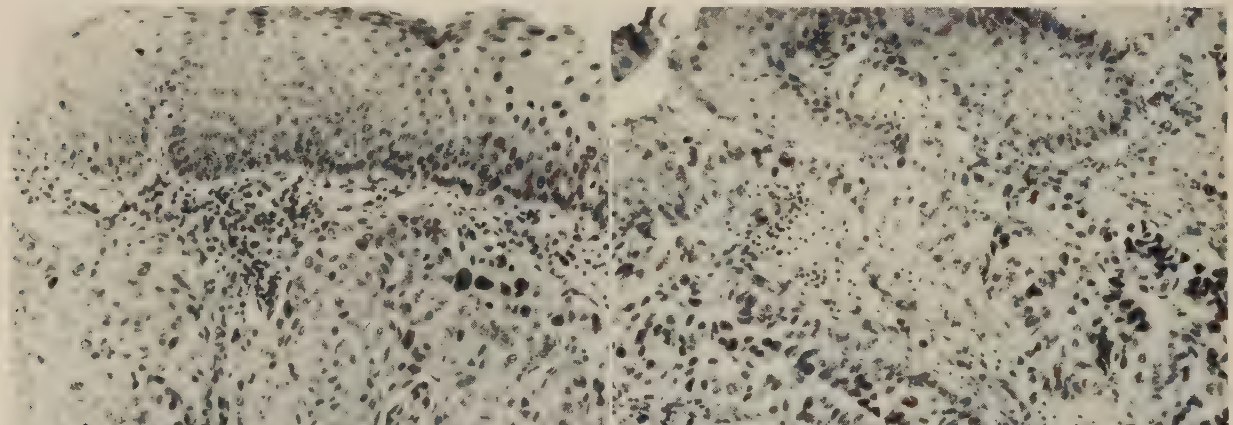


Nodular, polypoid tumor, distal third. 58 year old woman.

(All from E. Hirsch and P. Holinger, Chicago.)



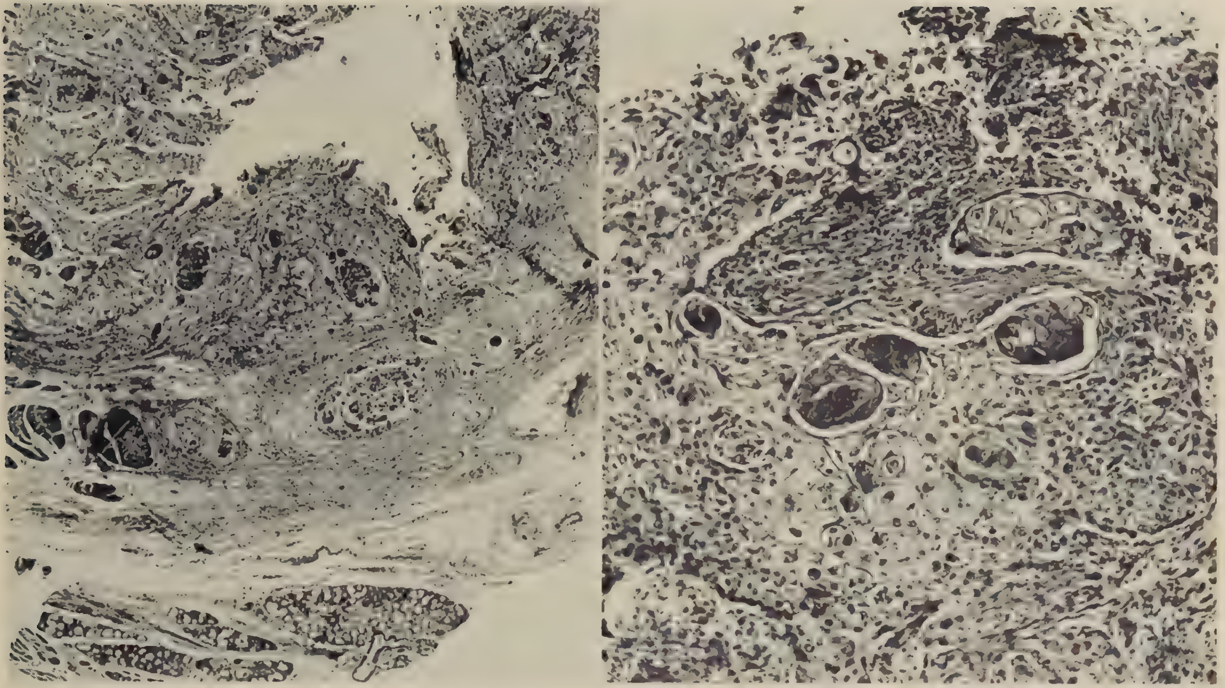
Early invasive carcinoma (entire lesion in section) arising in leukoplakia, which involves the epithelium above and below the tumor. These areas were interpreted by some as intraepithelial carcinoma. x12. At higher magnification, dyskeratosis and other features of leukoplakia are evident. Portion of infiltrating tumor at left. x70. (W. Putschar, Charleston, W.Va.)



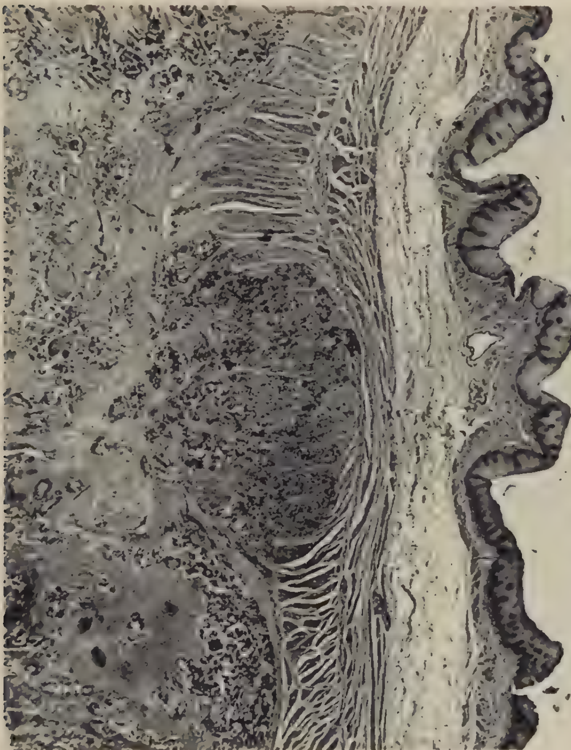
Esophagoscopic biopsy specimens. *Left:* from an epidermoid carcinoma obstructing lumen at level of cricoid in a 65 year old man with dysphagia for three months. x150. *Right:* adenocarcinoma from a fungating bleeding tumor 11 inches from upper teeth in a 44 year old man with dysphagia for a year. x130.(H.P. Mosher, Boston.)

ESOPHAGEAL FISTULA

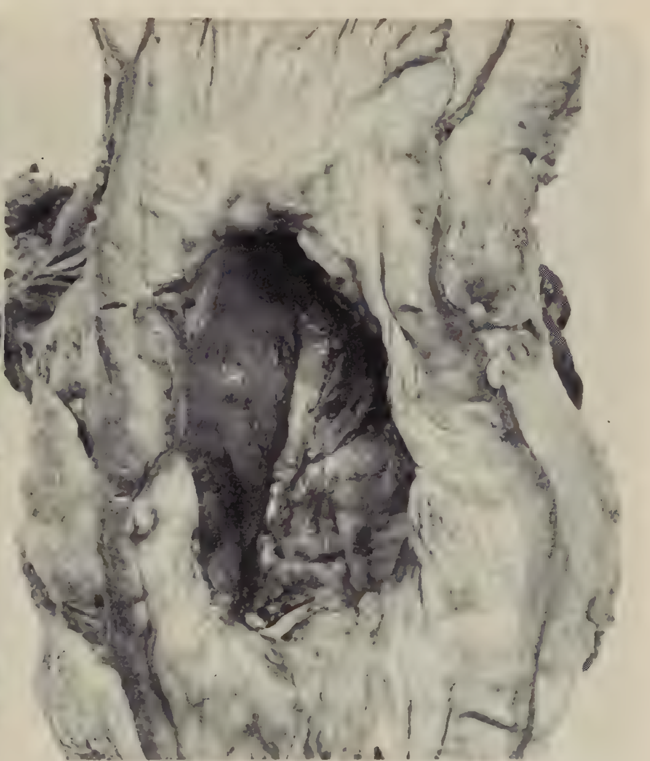
DUE TO CARCINOMA



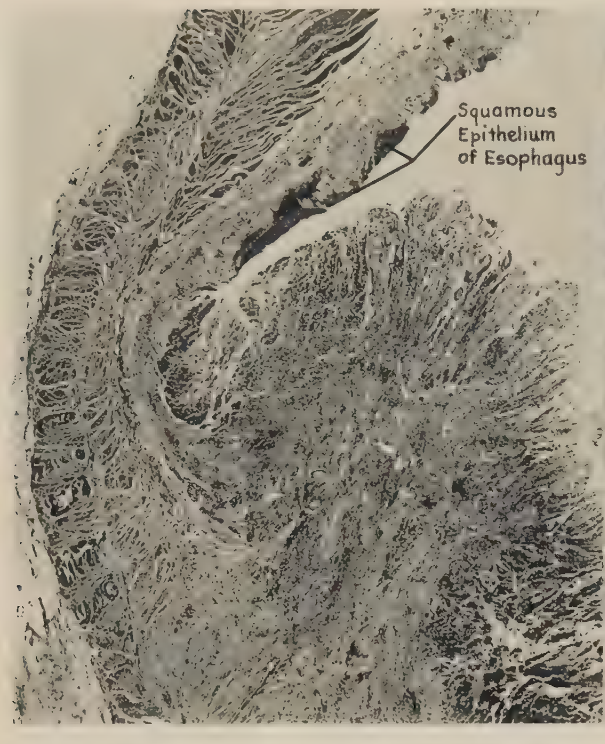
Esophagobronchial fistula in a 53 year old man with severe cough for two years. Epidermoid carcinoma involved entire middle third of the esophagus and extended to the coryna and upper left main bronchus. Well differentiated keratinizing tumor is invading the periesophageal tissues to the tracheal mucosa. The latter is not involved at this level. x16, x75.



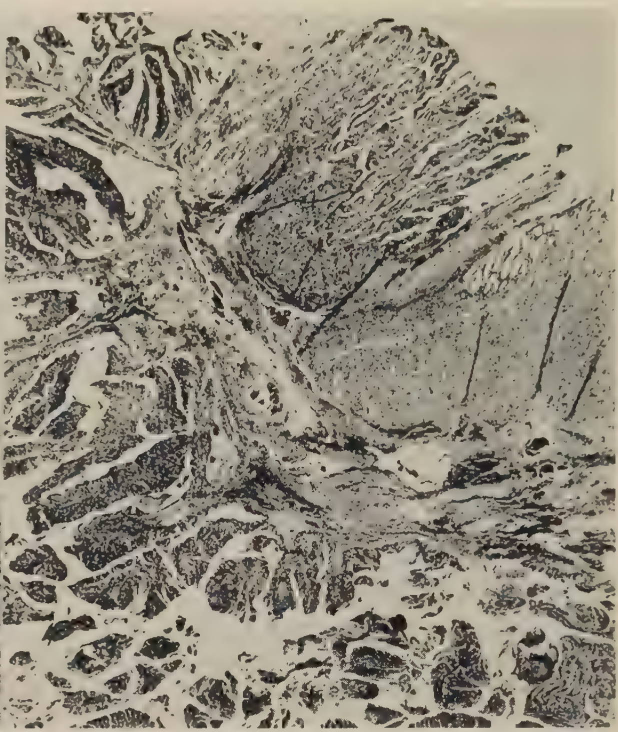
Bronchogenic carcinoma invading esophagus to the inner circular muscle layer. The poorly differentiated neoplasm has extensively infiltrated the adventitial tissues, and a large nodular mass is seen in the outer muscle coat. x9.



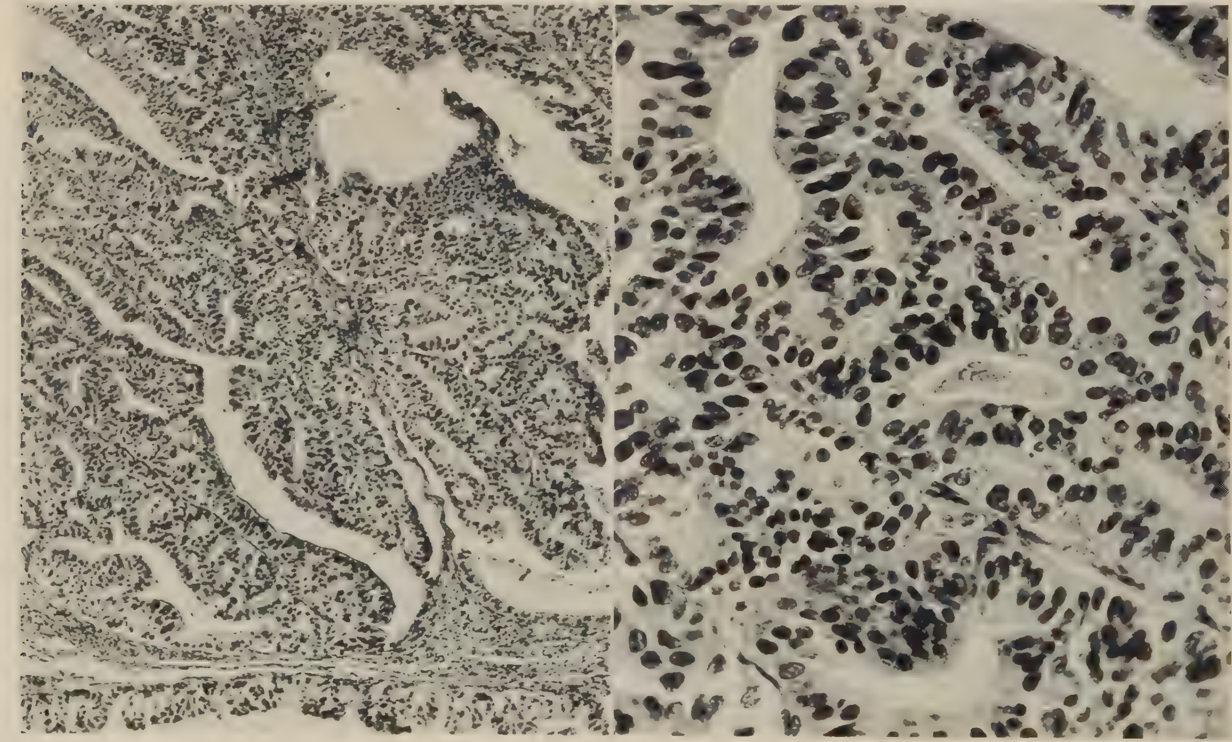
Bronchoesophageal fistula, produced by undifferentiated bronchogenic carcinoma in a 62 year old man, well until four months before death. Esophageal mucosa surrounds fistulous defect through which intact bronchial mucosa and a mass of tumor can be seen. (P. Holinger, Chicago.)



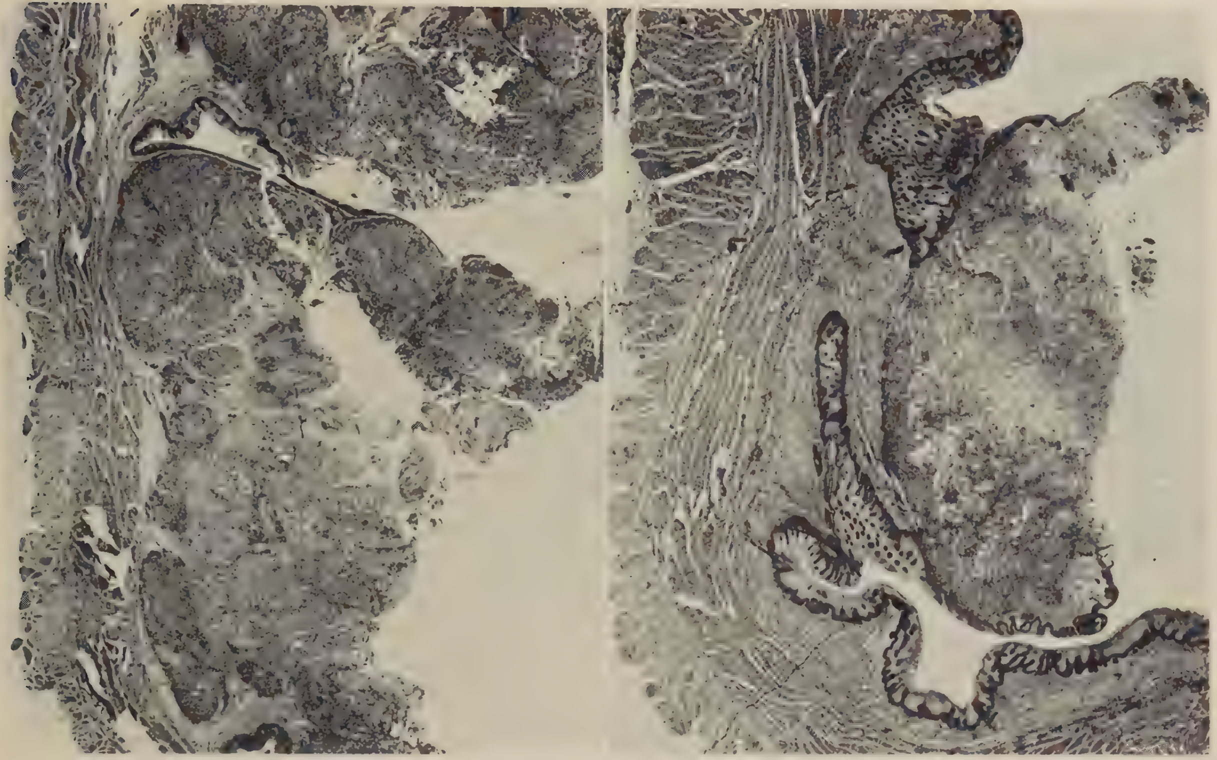
Adenocarcinoma, well differentiated, at cardioesophageal junction. Entire thickness of wall including muscle layers. Glandular pattern of edge of projecting fungating tumor is apparent at even this low magnification. x8.



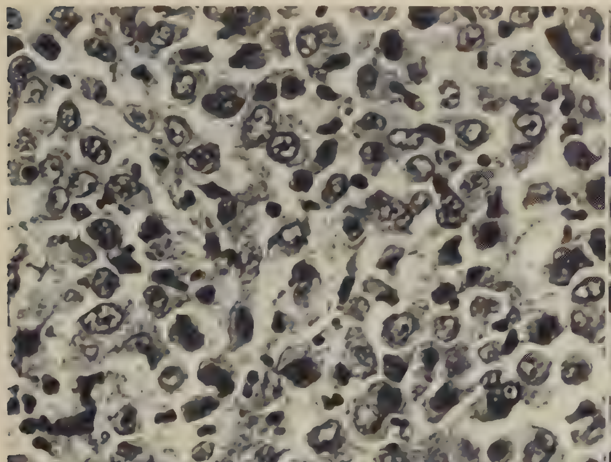
Papillary adenocarcinoma, infiltrating the cardioesophageal junction of a 46 year old man with increasing dysphagia for one and one-half years. At operation metastatic tumor was found covering the diaphragm and in 6 of 27 lymph nodes. x16.



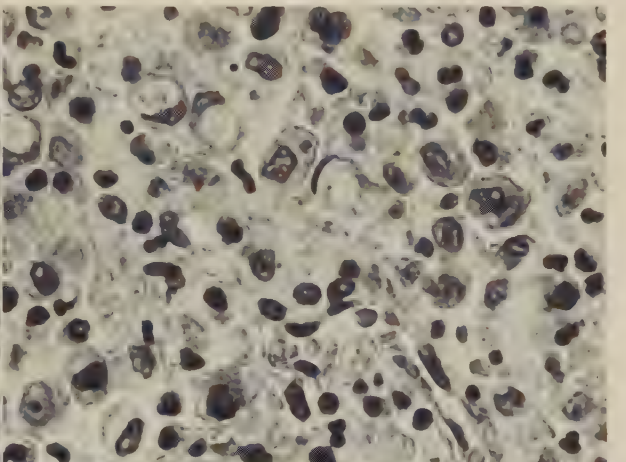
Papillary structure and glandular pattern are evident in magnified fields of case at *upper right.* Well differentiated neoplastic glands lined by columnar and cuboidal cells, often stratified. Moderate variation in size and shape; hyperchromatic nuclei; fairly frequent mitoses. x83, x395.



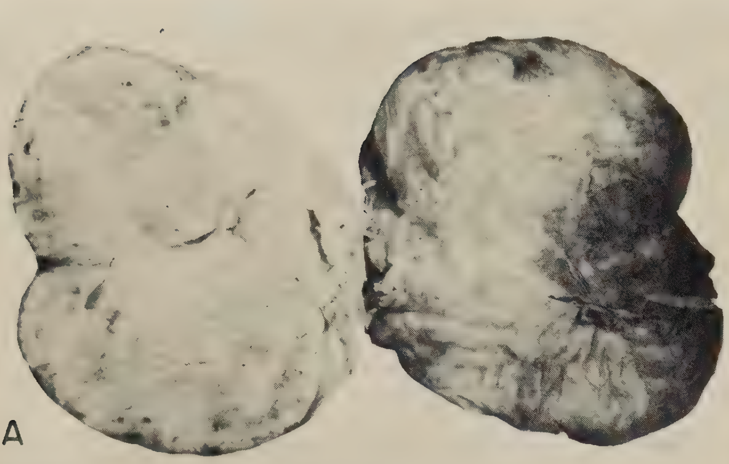
Adenocarcinoma, poorly differentiated, arising at cardioesophageal junction of a 30 year old man. Extensions to esophagus are illustrated. *Left:* nodular masses invading wall to muscle coat. x7. *Right:* linear superficial extension of the tumor in a section at a higher level of the esophagus. x8.

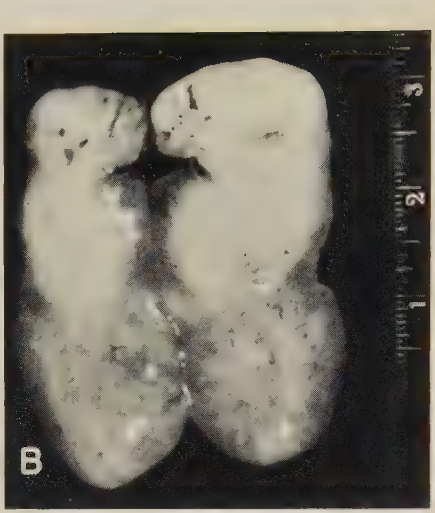


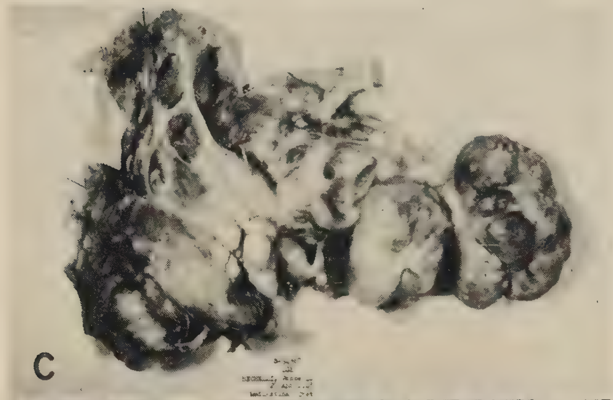
Poorly differentiated cells, loosely arranged, in most fields of the same tumor. Hyperchromatic nuclei; moderately abundant cytoplasm; numerous mitoses. x355.



Signet ring cells establish the glandular origin of the neoplasm. Though numerous in this field, they were found in only occasional small areas of the extensive tumor. x500.



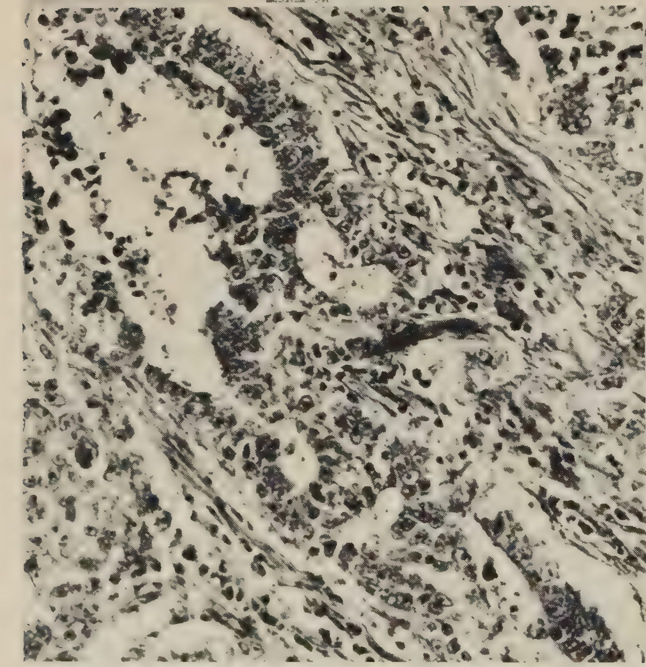




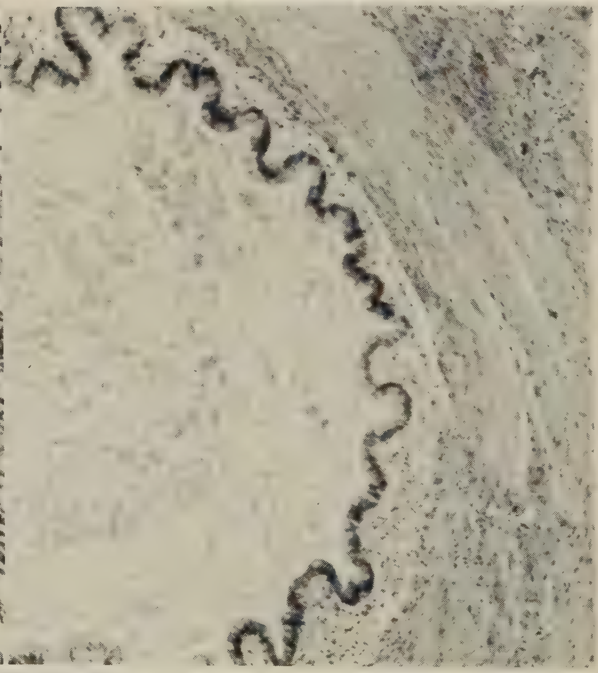
A. Neurilemoma (11x8 cm.), superior mediastinum, from a 38 year old woman. Well encapsulated largely solid tumor with fasciculated surface pattern, a few small cystic spaces and hemorrhagic areas.

B. Neurofibroma, mediastinum. Irregular mass which measured 9x4 cm.

C. Benign teratoma (2x15 cm.). Lobulated, well encapsulated, multiloculated tumor with polypoid and papillary excrescences projecting into the cystic spaces.

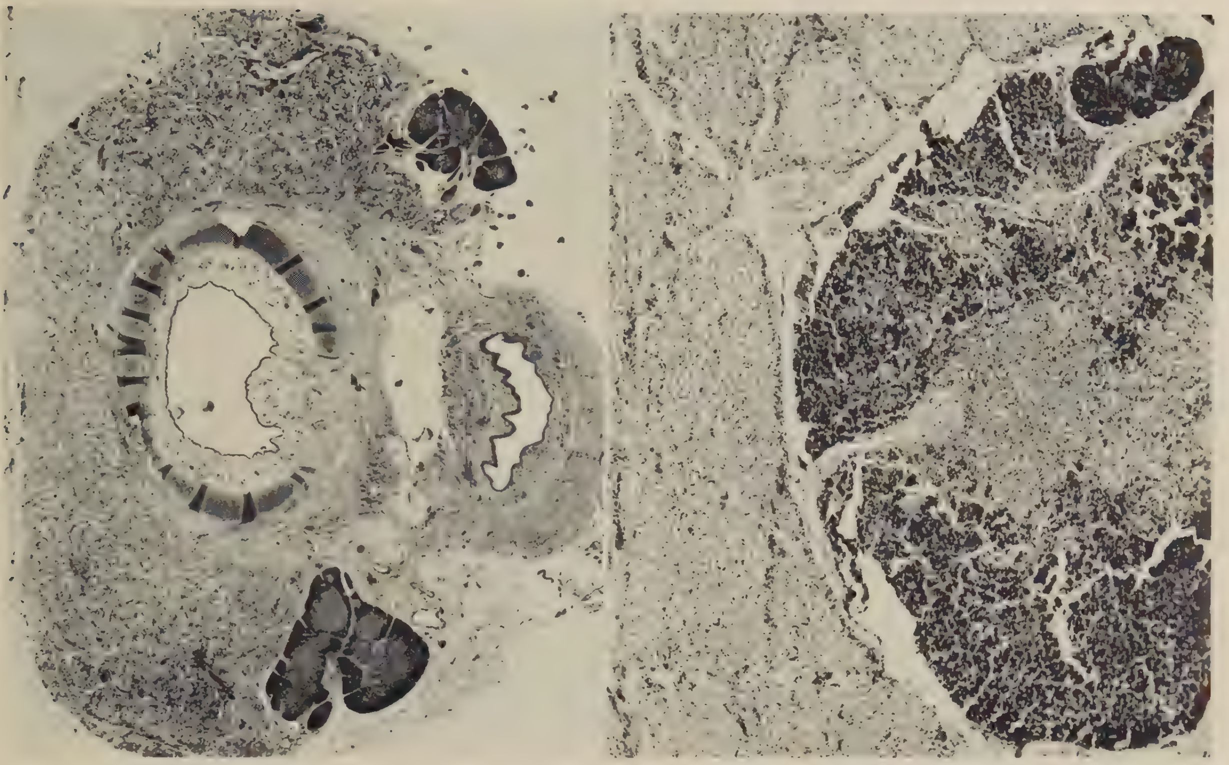


Malignant teratoma, from a 21 year old man who died two months after onset of cough and bloody sputum. Two large masses, 20x12x8 cm. and 18x14x9 cm., displaced heart and involved lungs. No metastasis. Glandular epithelium is frankly malignant. x230. (W.P. Butler, Shreveport, La.)

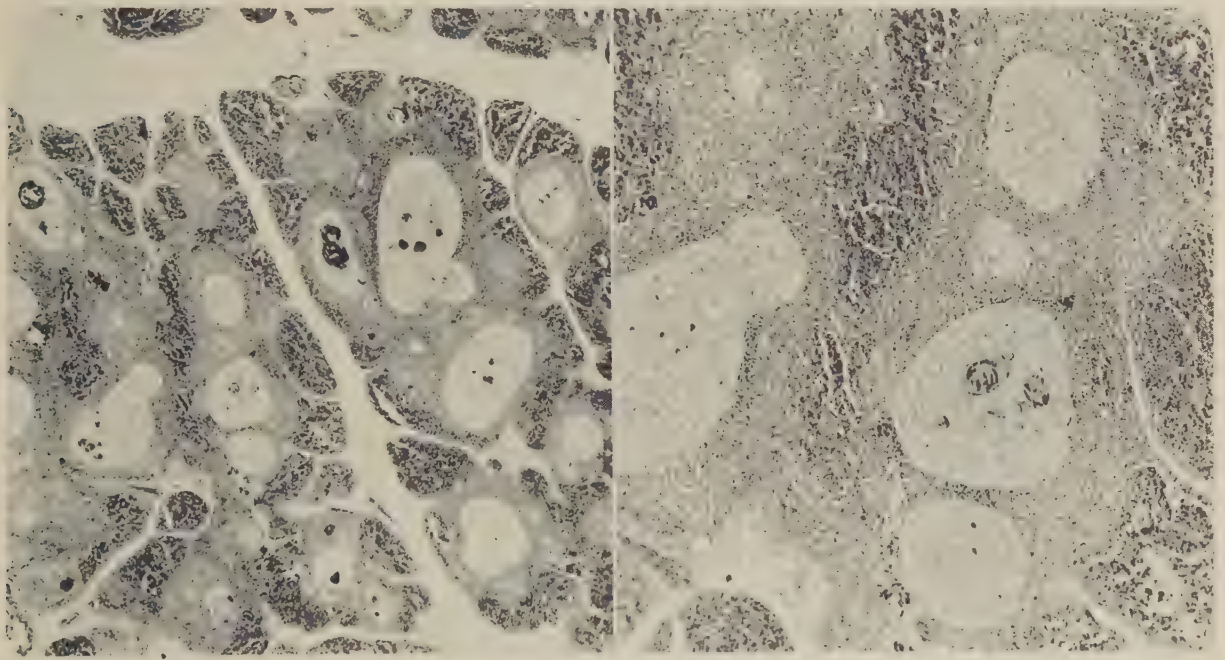


Benign teratoma (10x10x12 cm.), anterior mediastinum of a 22 year old man. Chest pain, dyspnea and cough of six months' duration. Cystic tumor contained skin elements, fat, cartilage, brain, and pancreatic tissue. Intestinal type mucosa with smooth muscle wall is illustrated. x100.

ABERRANT THYMUS–STATUS THYMICOLYMPHATICUS

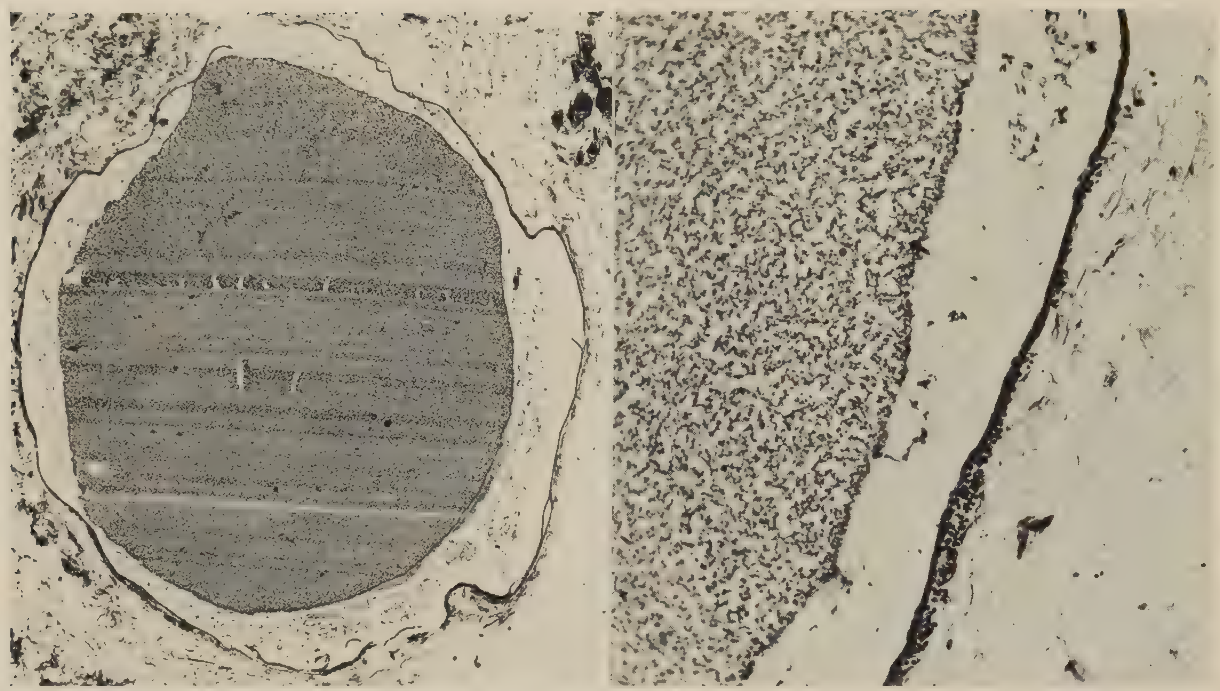


Thymic tissue in thyroid gland of infants. *Left:* transection, at level of the thyroid gland, through trachea and esophagus of an infant who died with erythroblastosis. Two black areas at right top and bottom are accessory thymus lobules (showing no erythropoiesis) at posterolateral borders of thyroid. Small pale areas medial to them are parathyroid tissue. x8. *Right:* thymic tissue with well defined cortex and medulla in thyroid–incidental finding in 6 month old infant. x48.

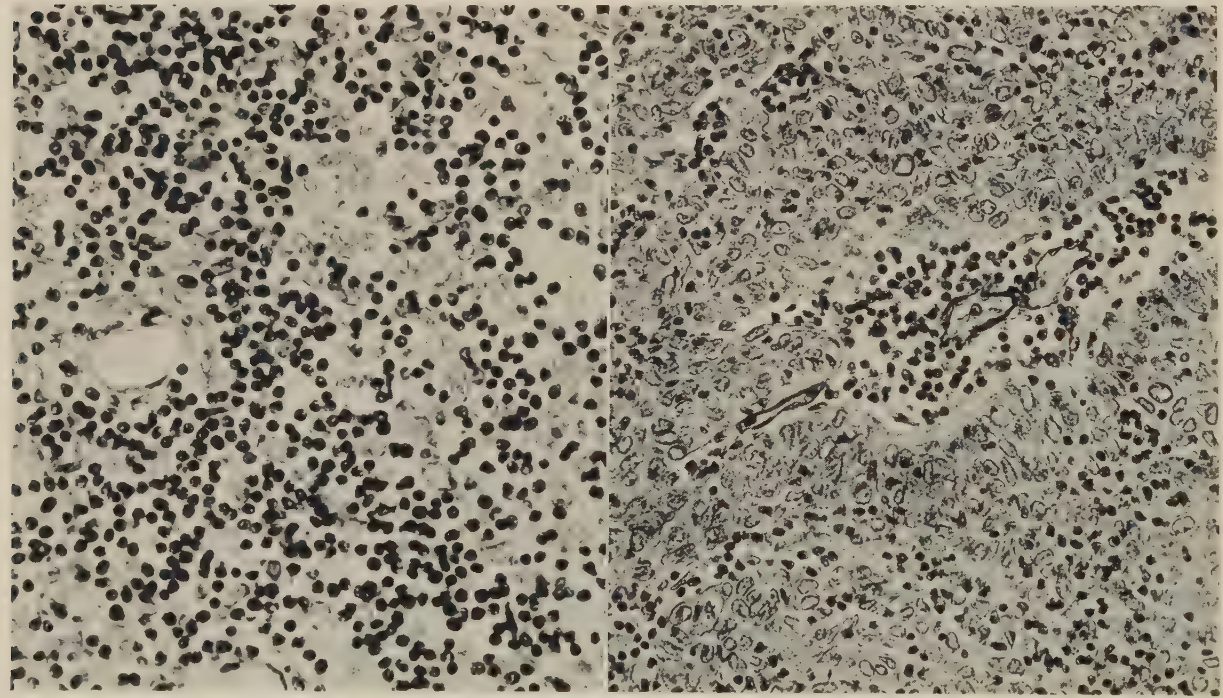


Status thymicolymphaticus(?). Sections from a 45 Gm. thymus of a 9 year old boy, who collapsed while playing and died a few minutes later. Unusually numerous, prominent bodies of Hassall, some with small central cysts and calcium deposits–evidence of pronounced degenerative change. x20, x52. Atrophy of the adrenals and a generalized lymphatic tissue hyperplasia with unusually prominent mesenteric lymph nodes and intestinal lymphatic tissue were also noted. Many doubt the concept of this condition as a pathologic entity.

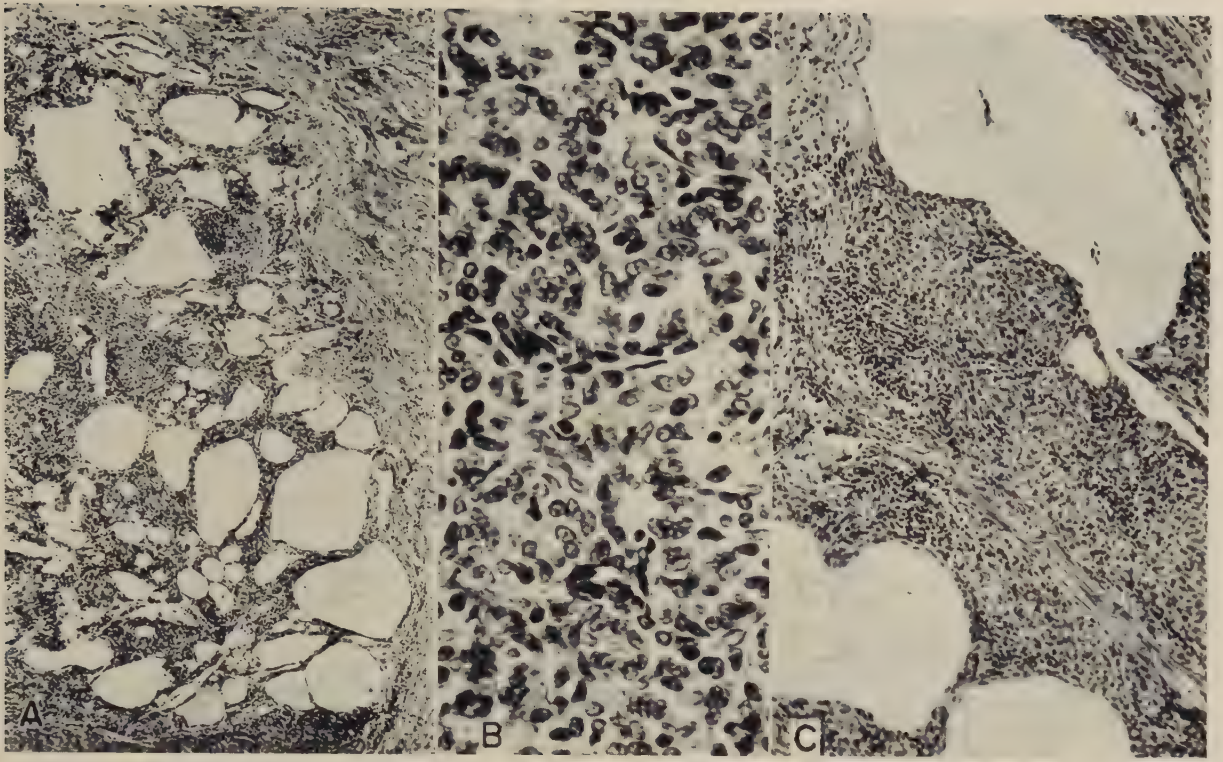
CYST–IN MYASTHENIA GRAVIS



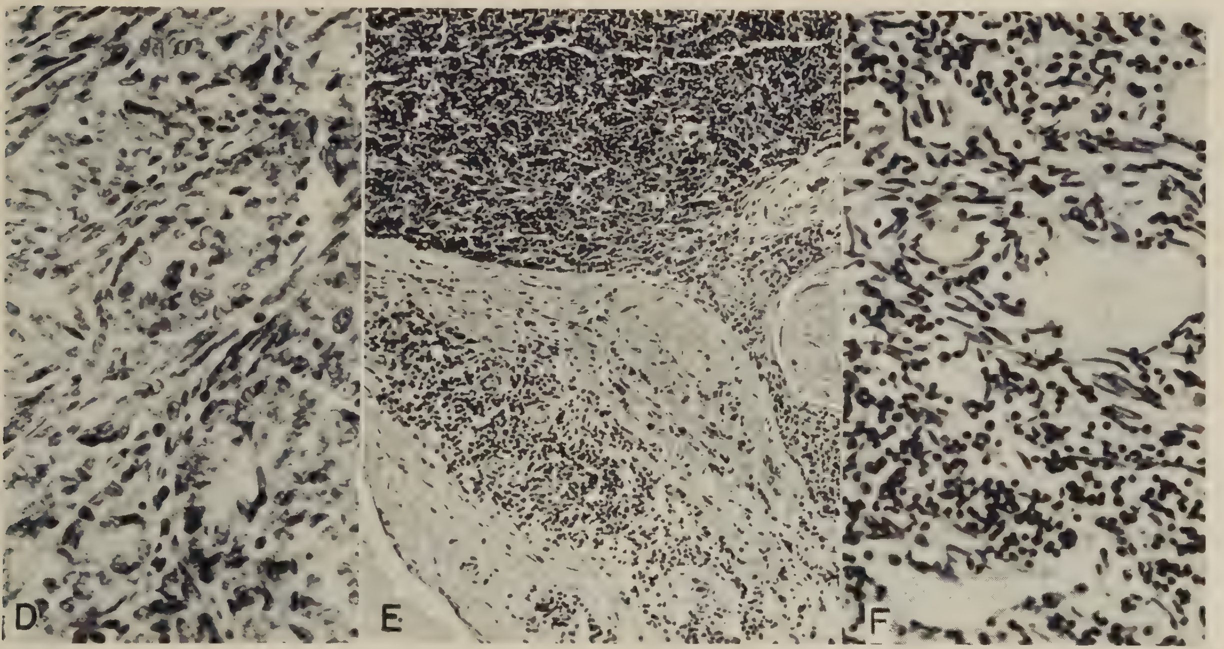
Cyst of thymus, less than 1 cm. in diameter, an incidental finding in 80 year old man. It is lined by closely spaced polyhedral or flattened cells, occasionally multilayered, that appear epithelial. x21, x125. The thymus shows involutional changes in illness and with increasing age after puberty. Note predominant fat tissue content of surrounding thymus.



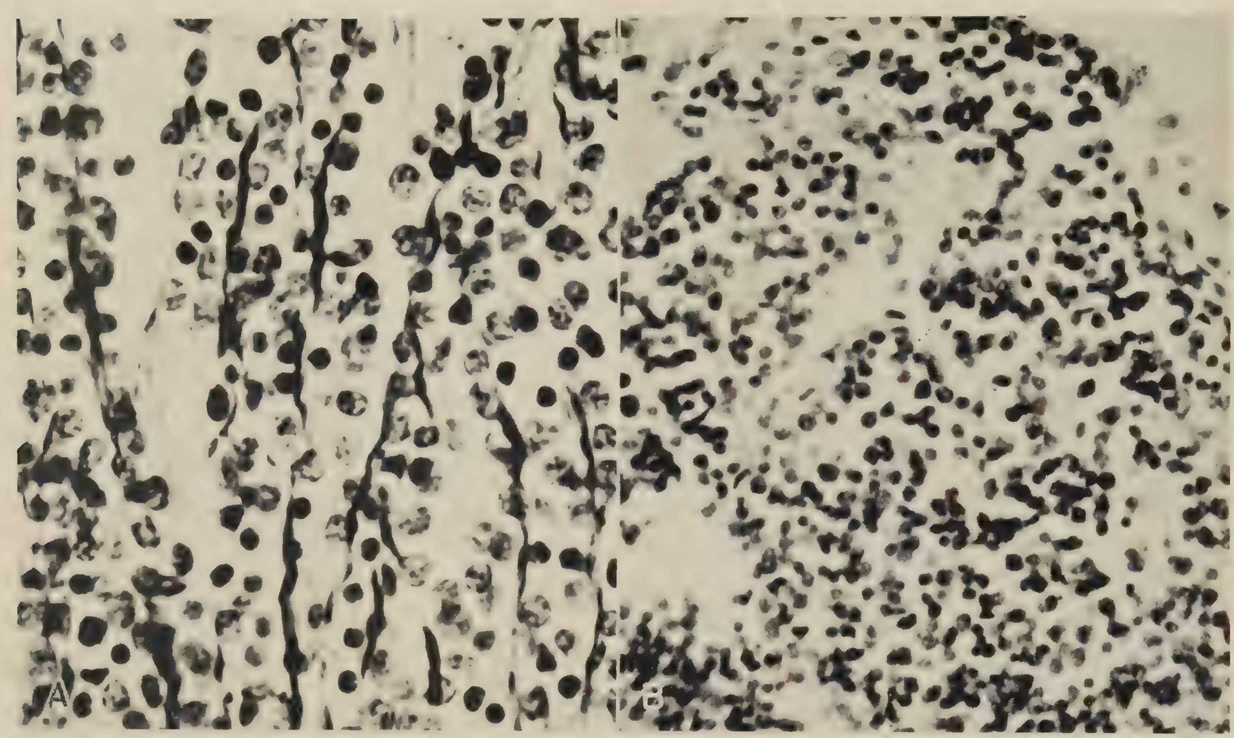
Thymoma in myasthenia gravis. A benign encapsulated thymic neoplasm occurs in 15 per cent of cases. *Left:* this field, characteristic of the majority of such thymomas, is from a well circumscribed, ovoid, anterior mediastinal mass, 6x4.5 cm., removed from a 37 year old man with myasthenia gravis for sixteen years. Large pale cells are intermingled with lymphocytes in a loosely fibrous and vascular stroma. The pale cells tend to group around capillaries. x450. *Right:* another case shows unusual prominence of the large pale cells, which assume a columnar form about the blood vessels. Lymphocytes are not prominent. Transitions to Hassall's corpuscles seen in other sections. x290. (L. Iverson, Wash., D.C.)



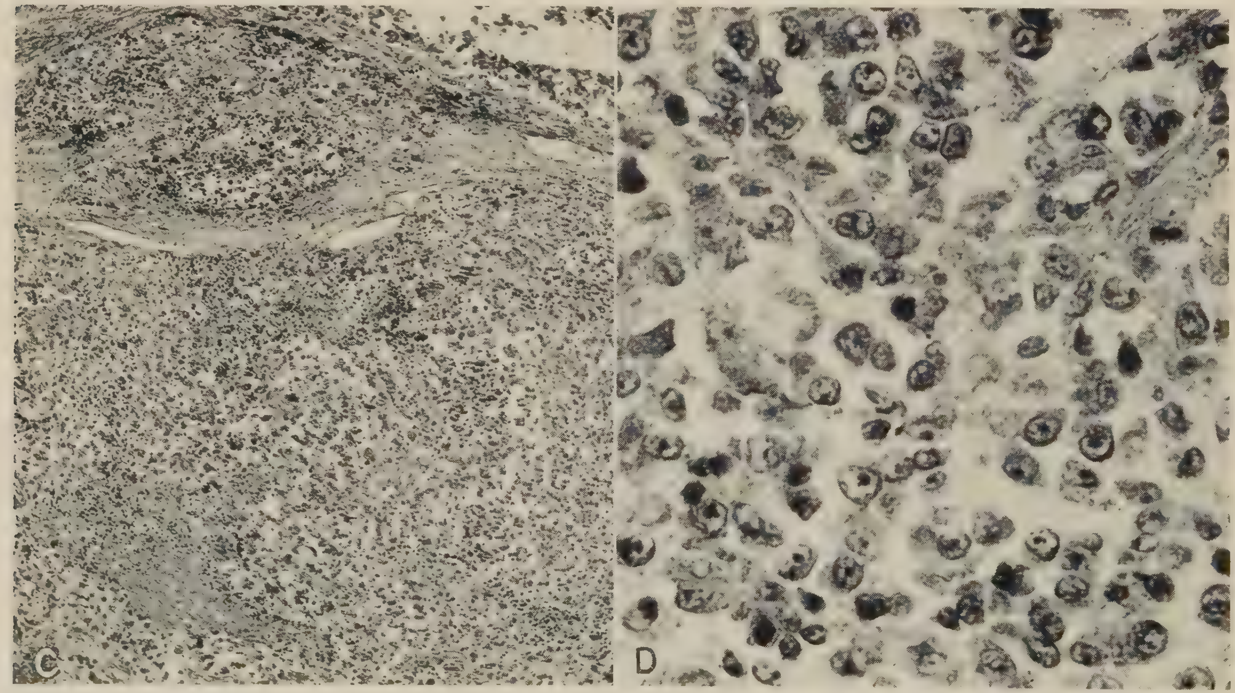
Encapsulated solid thymoma, 8x9x6.5 cm., removed from anterior mediastinum of a 71 year old woman. **A** and **C.** Small and large cystic spaces containing homogeneous acidophilic material, about which are spindle cells similar to the lining cells and, in **"C,"** projecting into a lumen. x62, x125. **B** and **D** *(below).* Whorled groups of cells (lymphangioendothelial?) compactly arranged adjacent to the spaces, interpreted as lymphatic vessels, and within the stroma of lymphocytes. x395. The lymphocytic component, inconspicuous in these fields, predominated in others.



E. Encapsulated partly cystic thymoma from 17 year old girl contained cavernous endothelium-lined channels; spindle-shaped cells about minute spaces among the lymphocytic cells; Hassall's corpuscles. x125. **F. Solid encapsulated tumor,** 7x9 cm., from 63 year old man. Equal proportions of spindle cells, often about channel-like spaces, and lymphocytic elements. x275. No suggestion of myasthenia gravis in these three cases. (A. Liebow, New Haven.)



Thymoma or malignant lymphoma? Enormous tumor (at anatomic site of thymus) in a 25 year old man extended up trachea and surrounded pericardium down to diaphragm. Direct extension to lung parenchyma, but no apparent metastasis. Grossly and clinically the tumor is thymoma; histologically it is questionable. **A.** Tumor cells resemble lymphocytes, but have a very suggestive reticulum cell relation to reticulin fibers. Silver impregnation. x860. **B.** In this extension to lung the tumor cells are lymphocytic and few fibers are seen. x405.



Malignant thymoma or reticulum cell sarcoma? Mediastinal mass in a 55 year old man extended up neck, invaded lung, and metastasized to hilar and supraclavicular nodes to produce a superior vena caval syndrome. Patient lived nine months after first symptoms. Location of tumor was chief reason for a diagnosis of malignant thymoma of epithelial type. **C.** Very cellular tumor. x62. **D.** Lack of cohesion of cells and their histologic structure suggest reticulum cells. x450.

CHAPTER 28

CYSTS, LYMPH NODES AND TUMORS OF THE NECK

Deep infections of the neck are of great surgical importance, and since the majority of them are extension of infections from the pharynx and mouth they are of concern to the otolaryngologist. Since they are, however, largely matters of surgical anatomy and pathogenesis, a detailed discussion is not within the province of this Atlas. The student is referred to the section on the pharynx for a review of some of the anatomic features and to Beck's articles for the details of pathogenesis.

The commonest infection in the neck is that of the lymph nodes. This usually remains localized, but when there is a fulminant suppuration, it may break loose into the surrounding tissues resulting in a more serious cellulitis. Next in frequency is extension of an infection beginning about the teeth, especially those of the mandible, as an osteomyelitis that erodes through the bone cortex. Least common, certainly since antibiotics have become available, are the infections that extend down from the mouth and pharynx along fascial planes. Three serious complications are possible from the deep infections—mediastinal cellulitis, thrombosis of the internal jugular vein and the carotid artery, and edema of the glottis.

CYSTS

Branchial cysts may arise in the lateral portions of the neck from inclusion, during development, of either ectodermal or entodermal elements from the branchial arches or the pouches. They produce nodules of various sizes, usually unilateral and located close to the angle of the mandible anterior to the sternocleidomastoid muscle. Occasionally the sinus has remained open on the skin surface or into the pharynx, either externally or internally, as a result of fistula from an abscess. Because of its location it has been claimed that the cyst arises through the persistence of the pericervical sinus.

The cyst may be lined by stratified squamous epithelium or ciliated pseudostratified columnar epithelium, usually with a varying amount of lymphatic tissue. In most instances the contents of the cyst are grumous material, accumulated debris of the cellular lining. If the wall is ulcerated, a foreign-body giant cell reaction will be evident, and if there is bacterial infection, purulent exudate will be included in the contents and will invade the wall. Ordinarily the cyst is encapsulated by well developed fibrous tissue.

The squamous cell carcinoma which sometimes arises in these cysts must be differentiated from metastasis of an occult cancer of the nasopharynx.

Hygroma cysticum colli is a multilocular cystic tumor most commonly seen in the lower portion of the neck, but occasionally in the axilla. Goetsch reported on the clinical and pathologic aspects of twelve cases in which one or both parts were involved. It is due to a developmental disturbance of the lymph sacs which appear in the neck in the early embryologic development of the lymph system. It is probable that they are sequestrated elements of the jugular sacs which have failed to connect with the normal lymphatic channels. The tumor usually appears in childhood and continues to grow, at times attaining a large size and even extending down into the mediastinum. It enlarges not only by the accumulation of fluid in the cystic spaces but by actual sprouting of the endothelium from the cyst walls. It is, therefore, in a sense, infiltrating.

Grossly, the tumor varies in size from 2 to 10 centimeters in diameter and is multiloculated. Histologically, the cysts are lined by a single layer of robust endothelium and are embedded in varying amounts of dense collagenous connective tissue. The content of the cysts is coagulated albuminous material, sometimes with small mononuclear cell accumulations. The specimen illustrated in the following plates was obtained from a 42-year-old white male who had had a painless swelling low on the right side of his neck for about a year. The specimen was the size of a lemon. It was unusual because it had in its stroma areas of neurofibromatous elements.

The tumor is not malignant and complete removal is usually sufficient for cure. It has been reported that the lesion in young children has been successfully treated by irradiation.

Included in the plates are illustrations of a case of congenital lymphangiectasis that involved the neck and tongue of an infant to such an extreme degree that surgical intervention was attempted to prevent starvation. The patient did not survive the radical procedure necessary for complete removal. The tumor was not the classic hygroma cysticum colli even though the lymphatics were involved, but actually was an example of hamartoma.

CERVICAL LYMPH NODES

A brief review of the pathology of the cervical lymph nodes is indicated because of their importance in differential diagnosis. The simplest cause for enlargement of cervical lymph nodes is infection, primarily of the mouth and pharynx. The nodes on one or both sides are involved, their position depending on the site of the primary lesion. It is only in severe pyogenic infections that actual suppuration occurs. The adenitis subsides promptly with the elimination of the primary condition.

In simple **adenitis** the sinusoids are dilated and contain an excess of cells which include polymorphonuclear leukocytes as well as large mononuclear cells. The usual diffuse increase in the lymphocytes blurs somewhat the nodular pattern of the node, and the cells of the exudate invade the capsule. This is particularly true in a pyogenic infection in which abscess formation in the body of the node is also possible. In chronic infections the reaction can simulate a neoplasm, especially when the architecture of the node is largely destroyed, when there is a minimum of exudate, and when there are basophilic macrophages that resemble tumor cells scattered through the lymphatic stroma. At times there may be scarring of the node and especially of the capsule which will be irregularly thickened by fibrous tissue. On the other hand, there may be marked hyperplasia of the follicles, simulating the giant follicular form of lymphoma. Evidences of inflammatory reaction, however, can usually be found—plasma cells, phagocytosis by reticuloendothelial cells, for example. These reactive nodes are frequently trials to the pathologist.

Of the **granulomatous inflammations** in the cervical nodes, TUBERCULOSIS is the commonest. It occurs primarily in children and young adults and may involve a whole chain of nodes, usually on one side. The bovine strain of tubercle bacillus has been responsible for most infections of this type, which are far less frequent since effective measures for eliminating contamination of milk have been instituted. This lesion is the scrofula or "king's evil" of the old days.

Pathologically, the lymph nodes are more or less involved by typical tubercles which, when confluent and caseous, are evident grossly. Sometimes the nodes show evidence of regression of the infection with fibrosis and calcification. When the caseation is particularly active it may extend beyond the limits of the node, involve the skin, and break through the surface. The skin becomes secondarily infected with tubercle bacilli, producing the dermatologic entity SCROFULODERMA.

In secondary SYPHILIS the cervical lymph nodes share in the general lymphadenopathy. The enlargement is not as great as in tuberculosis, the nodes are smaller, discrete and shotty in consistency.

Histologically, the architecture of the node is definitely blurred, and there are areas of reticulum-cell hyperplasia, at times suggesting early tubercles or sarcoid. A high content of plasma cells will be found in the lymph tissue, and the blood vessels will usually exhibit varying degrees of the typical syphilitic vasculitis. Often the reaction is much less specific, and without the history or the demonstration of *Treponema* in the node, diagnosis from the histologic appearance is not possible.

Cervical lymph nodes may be the seat of the typical granulomatous reaction in TULAREMIA when the site of infection is about the face. This produces a chronic, low grade reaction that may last for months, with periods of exacerbation of the general symptoms as well as of the lymph node reaction.

The lesion consists of a granulomatous reaction with rather large oval or stellate collections of histiocytes (epithelioid cells) that are undergoing a granular type of necrosis in the center of the mass; around the necrotic material is a zone of palisaded histiocytes surrounded by lymphocytes. This form of tubercle is indistinguishable from that of lymphogranuloma venereum and several other specific infections, and it is only by the history and serologic studies that a diagnosis can be established.

The fungus diseases, ACTINOMYCOSIS and BLASTOMYCOSIS, are not primary infections of the lymph nodes but they can involve them secondarily from infections of the neighboring skin and soft tissues. HISTOPLASMOSIS, however, is a primary infection of the reticuloendothelial cells and the cervical lymph nodes may share in this systemic infection. Pathologically, it is characterized by a diffuse infiltration with histiocytes in which *Histoplasma capsulatum* can be demonstrated. (See Chapter 12.)

Infectious mononucleosis (glandular fever) is a febrile condition usually of children, which gives some evidence of being contagious. It is characterized clinically by enlargement of cervical and other peripheral lymph nodes, leukocytosis, and general malaise. Enlargement of the spleen is a common manifestation. In the blood a large, atypical, vacuolated lymphocyte-like cell, the Downey cell, is the characteristic cell of the disease. An important diagnostic procedure is the demonstration of the so-called heterophil antibody. The disease may run a protracted course but usually terminates favorably, although there are several known instances of death from rupture of the spleen and others in which fatal nervous system involvement of the Guillain-Barré type has occurred.

Of importance is the fact that the tonsils share in the reaction. They become moderately enlarged and show a propensity to ulcerate, in such a way, in fact, as to raise the question of leukemia or agranulocytic angina. The former is the more disturbing because the blood may show a high leukocytosis that with the atypical cells can be misinterpreted as a leukemia. Another disturbing clinical feature is the swelling and ulceration of the gingivae that can also simulate the reaction to more serious blood diseases.

Histologically, the node architecture is blurred by the proliferation of lymphocytes and by the presence of the same large basophilic cell that is the characteristic feature of the blood picture. Small groups of these cells are also a feature of the tonsillar reaction. The cells usually infiltrate the node capsule. Custer and Smith found that similar invasion, weakening the splenic capsule, accounted for the rupture of the spleen. The typical cells are not restricted to the lymphoid structures, but are present in the parenchyma of the liver, kidneys, appendix and other organs.

TUMORS

There are various classifications of tumors primary in the lymphatic tissues; some of them that attempt differentiation on a histogenetic basis are very complicated. Callender provided a good working classification that is still used with minor modifications by the Lymphatic Tumor Registry. The classification of Gall and Mallory is somewhat more elaborate. On the other hand, as experience has accumulated, some pathologists have come to believe these tumors all stem from the same cell–the reticulum cell. There are, however, clinical entities, and a certain degree of pathologic differentiation is possible. Hodgkin's disease usually runs an orthodox clinical course and maintains more or less recognizable histologic characteristics. These certainly can be differentiated from full-blown lymphatic leukemia and from the Brill-Symmers syndrome. The difficulty arises in the fact that the tumors do not remain true to form and there is considerable intermingling of cell types in a given tumor. For our purposes it is sufficient to remember that the lymphatic tissue is made up of two main elements, the reticulum cells and the cells of the lymphoid series. Tumors may arise in either one of these tissues. There are three basic malignant neoplasms of the reticulum cell: reticulum cell sarcoma, monocytic leukemia, and Hodgkin's disease. When the tumor is confined to the tissues the first term is applicable, and when in addition to the local tumor there are tumor cells in the blood stream, it is monocytic leukemia.

Reticulum cell sarcoma arises from the cells of the reticuloendothelial system, especially those of the lymphatic tissue but also those of the bone marrow. It is rare in the nose and sinuses but not uncommon in the pharynx because of its large supply of lymphatic tissue elements. It is seen most commonly in late middle life. It manifests itself by focal or diffuse enlargement of the pharyngeal mucosa or tonsillar tissue. It tends to ulcerate early and to be complicated by secondary infection. Occasionally it is systemic in distribution as are other lymphomas, and along with the pharyngeal tumor, enlarged lymph nodes will be found in other parts of the body. It does not metastasize as freely as do other malignant tumors.

Microscopically, the tumor consists of rather uniform polyhedral cells that have relatively large and hyperchromatic nuclei, differing from the epithelial cell in the relatively smaller amount of cytoplasm and in the denser nuclei. Mitoses are readily found and among these will be abnormal forms. There may be considerable variation in the size and shape of the cells and some with two or more overlapping nuclei are encountered. These latter resemble very closely the Dorothy Reed cell of Hodgkin's disease, in fact the latter is generally considered to be a variant of reticulum cell sarcoma. The cells of the tumor do not have the cohesiveness of epithelium.

It is a function of normal reticuloendothelium to form fine reticulin fibrils and this is retained to a greater or less degree in the tumors. These fibrils are a means of differentiation from the transitional cell epithelial tumor with which it is readily confused. In silver preparations the reticulin is seen as fine fibrils in close relationship to the cells, and under favorable circumstances the individual cells can be seen suspended like aspen leaves by delicate fibrils from the largely reticulin trabeculae. In the more rapidly growing and pleomorphic tumors there is little or no demonstrable reticulin except the few coarse fibrils that remain from the original tissue. The cells are diffuse masses with little stroma but with sufficient vascular elements to prevent much necrosis.

Hodgkin's disease is still considered by some pathologists and clinicians to be a definite clinical and histologic entity. Others, more recently, think it is simply a variant of reticulum cell sarcoma. It does have certain clinical and pathologic characteristics that set it apart although the basic cell is the reticulocyte and the end result is the same in both tumors. Hodgkin's disease is seen more commonly in young adults, especially in the male, typically as an enlargement of the cervical lymph node on one or both sides. It may manifest itself, however, first in lymph nodes of other parts of the body, particularly those of the mediastinum and abdomen. The nodes in the early stages are discrete but eventually tend to coalesce into a fused fibrotic mass. In the active stages there are constitutional symptoms consisting of irregular fever, skin lesions, and a slight rise in blood eosinophils.

Histologically, the picture varies considerably. In the early stages the lesion may be of a granulomatous type and difficult to distinguish from early tuberculosis or sarcoid. It was this characteristic that led to the early belief it was the result of tuberculosis. But eventually the pleomorphism of the reticuloendothelial cells becomes obvious and the large, bizarre multinucleated cell (Dorothy Reed-Sternberg cell) so characteristic, appears. Usually eosinophils are increased and fibrosis is present in varying degree. This is the granulomatous form of Hodgkin's disease. The increase in connective tissue may dominate the picture, when it is spoken of as sclerosing Hodgkin's disease. The process may remain confined to the lymphatic tissue, including the spleen, but frequently terminates as sarcoma, metastasizing to the internal organs and also the meninges. A confusing early variant of the histology is the presence of exudate and necrosis. These make it difficult for the pathologist to differentiate it from an infection.

Tumors involving the lymphocyte element appear in several pathologic and clinical forms, with and without leukemia. **Lymphosarcoma** or **diffuse lymphocytoma** is the form in which there is complete obliteration of the node architecture, but the cells are generally recognizable as lymphocytes. These cells invade the capsule and surrounding areolar tissue. On closer examination it can be seen that the cells vary somewhat in size, shape, and particularly in the proportion of cytoplasm to nucleus. Mitotic figures are readily found and there are some larger reticulum-like cells. This tumor remains confined to the lymphatic tissue (lymphocytoma aleukemic), it may metastasize (lymphosarcoma), or it may be accompanied by leukemia (lymphatic leukemia). In the last two types there will be deposits in various organs. Lymphosarcoma in older individuals usually runs a chronic course, particularly if it is adequately treated by radiation. It has been called the benign lymphoma of the old. In young children, however, it can be fulminant and terminate in death in a matter of several months.

The other type of lymphocytic tumor is the so-called **giant follicular lymphocytoma (Brill-Symmers disease).** In this condition the lymph nodes and possibly the spleen are enlarged through hypertrophy and hyperplasia of the follicles, particularly of the so-called germinal centers. This is difficult sometimes to differentiate from the hyperplastic reaction to inflammations, but the cells of the germinal centers exhibit their neoplastic character by variation in size and chromatin content and practically no evidence of phagocytosis. In the inflammatory hyperplasia, however, the cells of the germinal centers are actively phagocytic and they are more uniform in size and character.

The stage of nodular hyperplasia may persist as such for years, but it usually terminates in frank malignancy—lymphosarcoma, reticulum cell sarcoma, or Hodgkin's disease.

Secondary Tumors.—The tumor most frequently metastatic to the cervical lymph nodes is carcinoma. The clinical behavior of carcinoma of the nasopharynx in this regard has already been mentioned. Carcinomas of the tongue, lips and oral mucosa eventually metastasize to the cervical nodes. One practical point should be mentioned—enlargement of cervical lymph nodes in association with a carcinoma of the lip, for example, does not necessarily mean tumor metastasis. An ulcerating tumor secondarily infected can be the source of adenitis.

A special clinical and pathologic entity is the presence of thyroid tissue in cervical lymph nodes. This is explained in the section on the thyroid gland.

TUMORS OF OTHER NECK TISSUES

In addition to the tumors that occur in the organs and glands of the neck there are others that arise in the tissues. There are several instances of **rhabdomyosarcoma.** The one included in the illustrations was from a 60-year-old colored man, who claimed he had had a "kernel" in his neck for 40 or 50 years. The tumor was the size shown in the clinical photograph when he came under observation. The mass, weighing 1100 grams, was removed, but the patient died of general metastasis two months later. This case was reported by Harper and Feder. **Tumors of neural origin** occasionally are seen. These are peripheral ganglioneuromas that may include neurilemma, neurofibril and nerve cell elements. Gore included several tumors from the neck among the group of primary malignant tumors of nerve that he reported. Other tumors arising in the neck are also included in the group of peculiar organoid neoplasms reported by Smetana and Scott and classed by them as malignant tumors of nonchromaffin paraganglia.

Another interesting but rare entity is the brown-fat tumor called **hibernoma** because of the similarity of the cells to those in the hibernating organs of lower animals. The tumor occurs most commonly in the interscapular region, but it has been reported in other parts of the neck.

Attention is called to the occasional persistence in the neck of portions of Meckel's cartilage. These remains may be unaccompanied by cyst formation. Naturally they are evident at birth.

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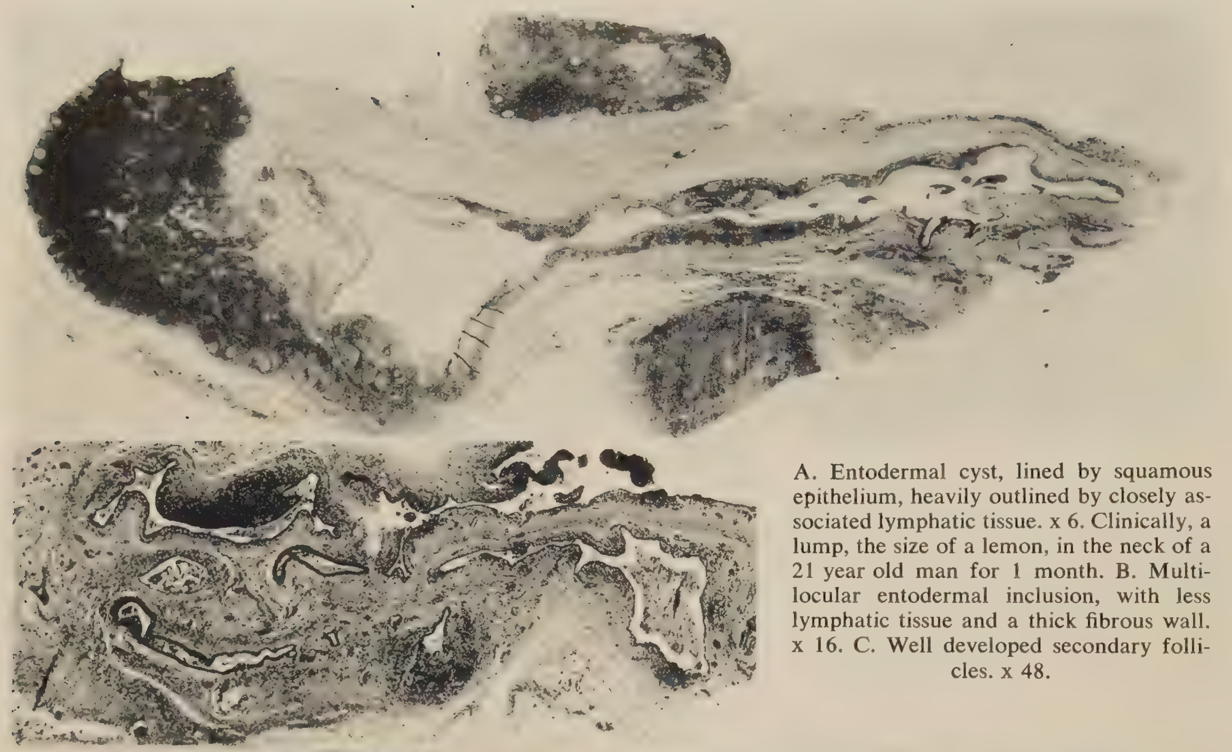
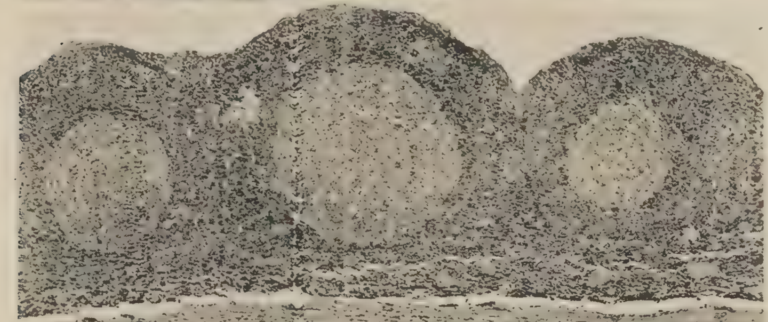
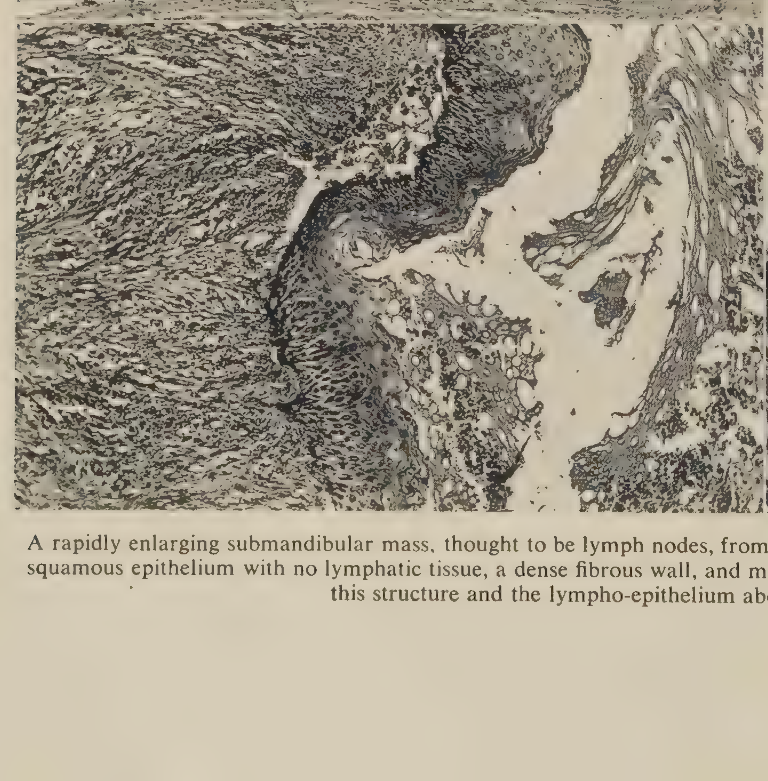
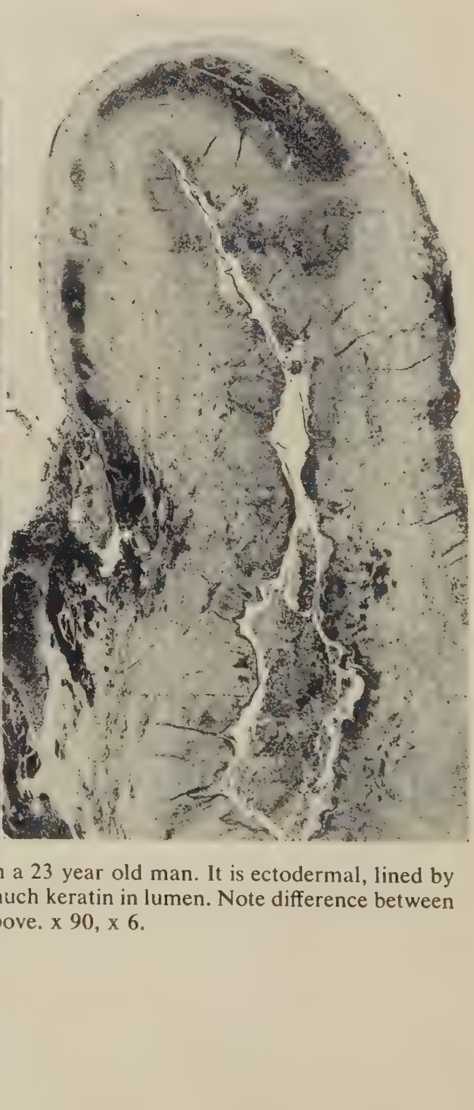


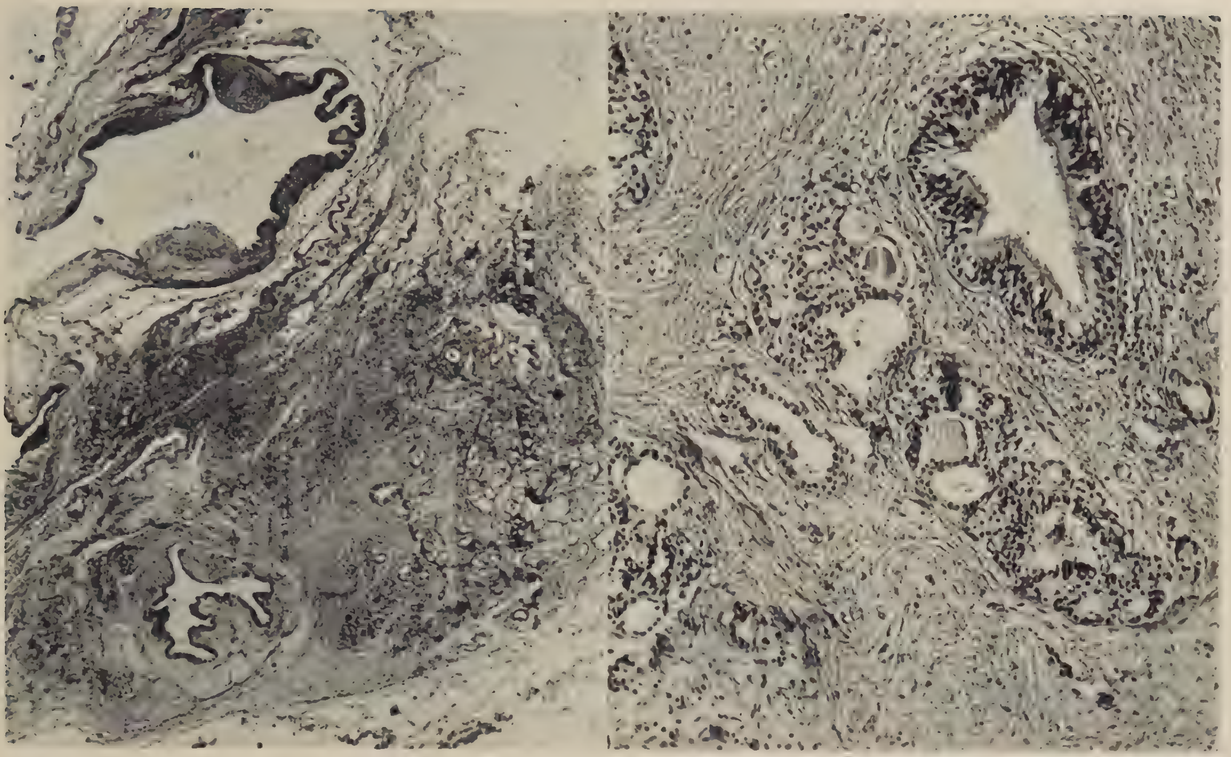


A. Entodermal cyst, lined by squamous epithelium, heavily outlined by closely associated lymphatic tissue. x 6. Clinically, a lump, the size of a lemon, in the neck of a 21 year old man for 1 month. B. Multilocular entodermal inclusion, with less lymphatic tissue and a thick fibrous wall. x 16. C. Well developed secondary follicles. x 48.

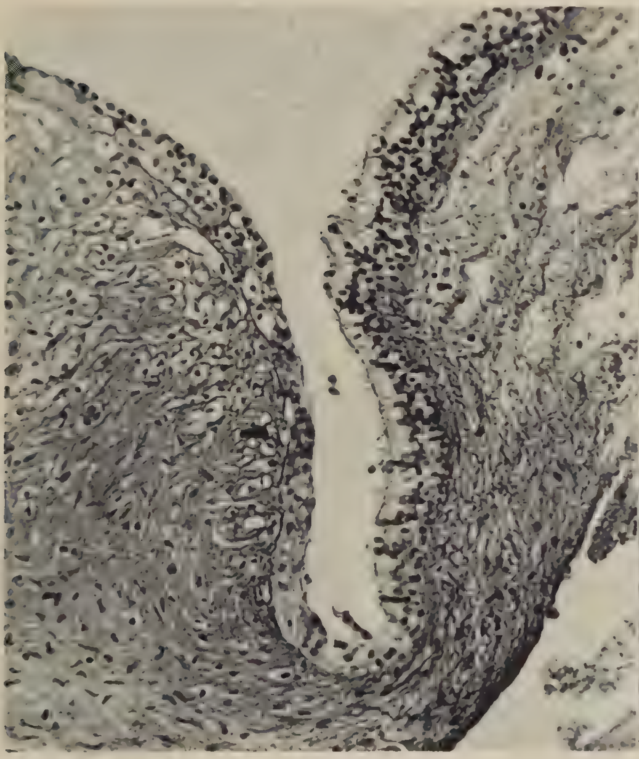




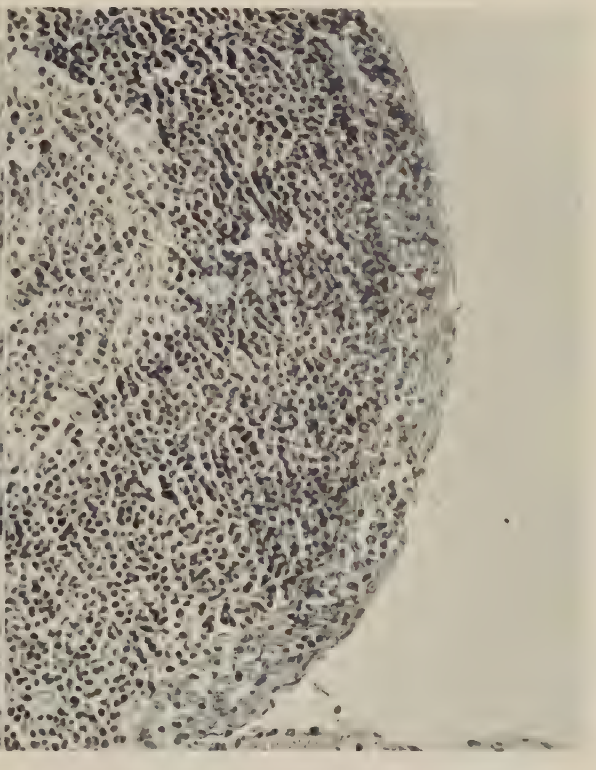
A rapidly enlarging submandibular mass, thought to be lymph nodes, from a 23 year old man. It is ectodermal, lined by squamous epithelium with no lymphatic tissue, a dense fibrous wall, and much keratin in lumen. Note difference between this structure and the lympho-epithelium above. x 90, x 6.



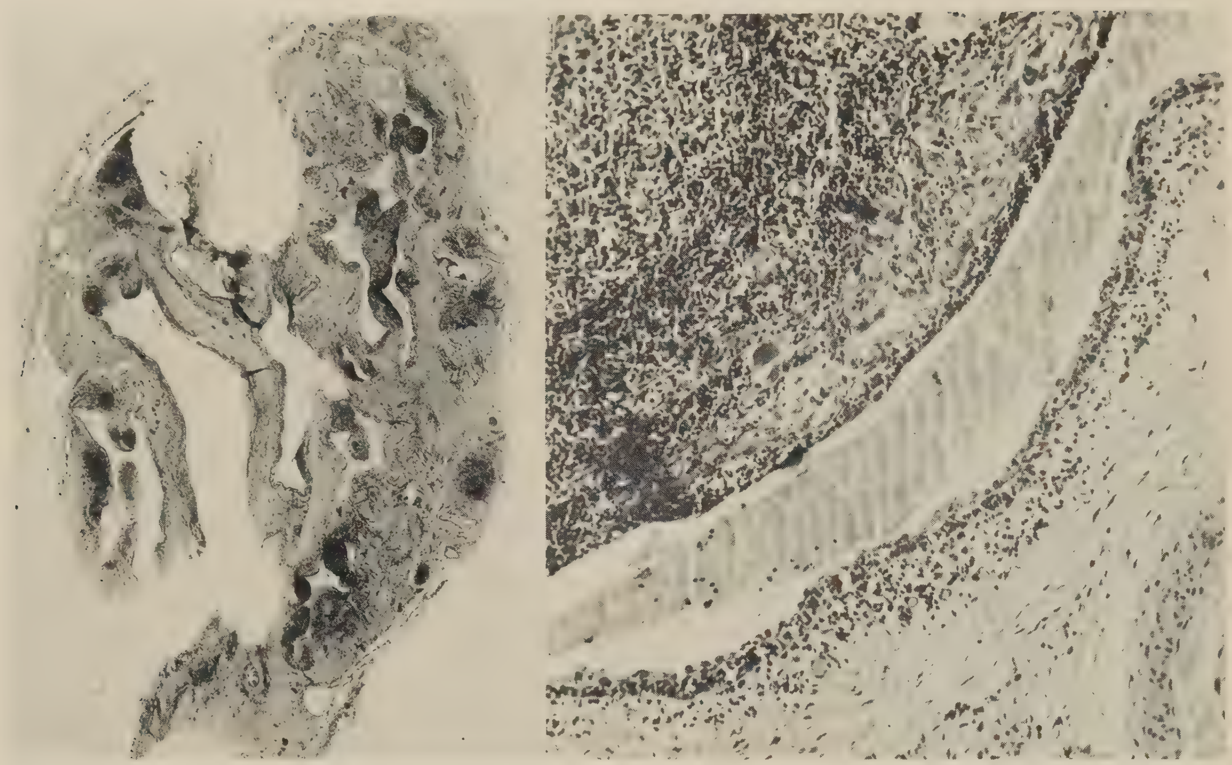
Probably a branching thyroglossal cyst, containing aberrant thyroid but no lymphatic tissue. The larger space is lined by squamous and respiratory epithelium. A twig lined by respiratory epithelium and partially surrounded by thyroid, in area at lower right. This portion is certainly thyroglossal. x 15. Thyroid acini, some containing colloid, x 115.



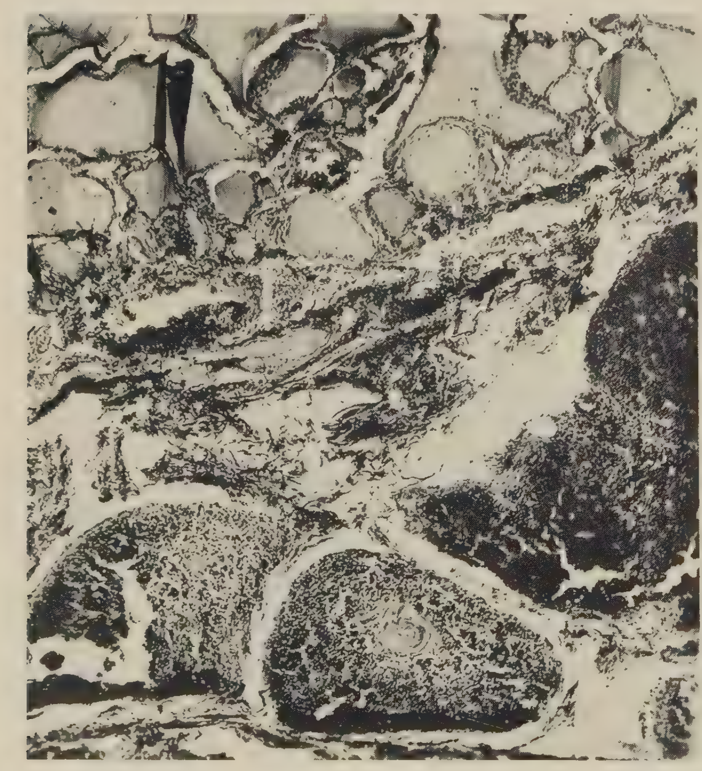
Schneiderian respiratory epithelium lining the large cyst seen at left, above. x 163.



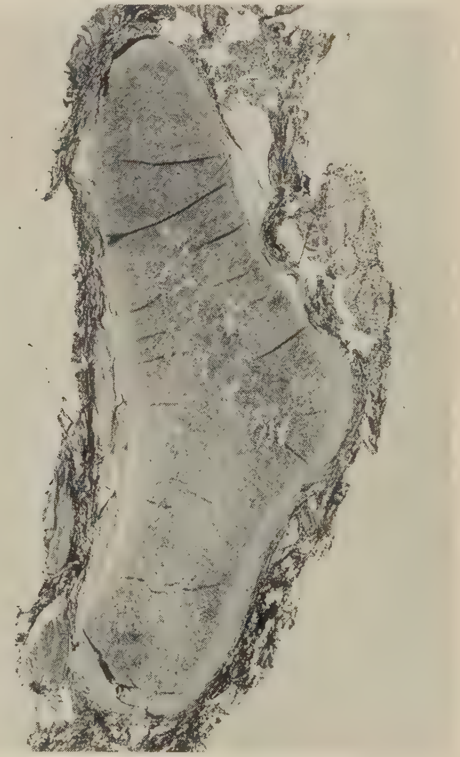
Lymphoepithelium from an entodermal branchial cyst. x 235.



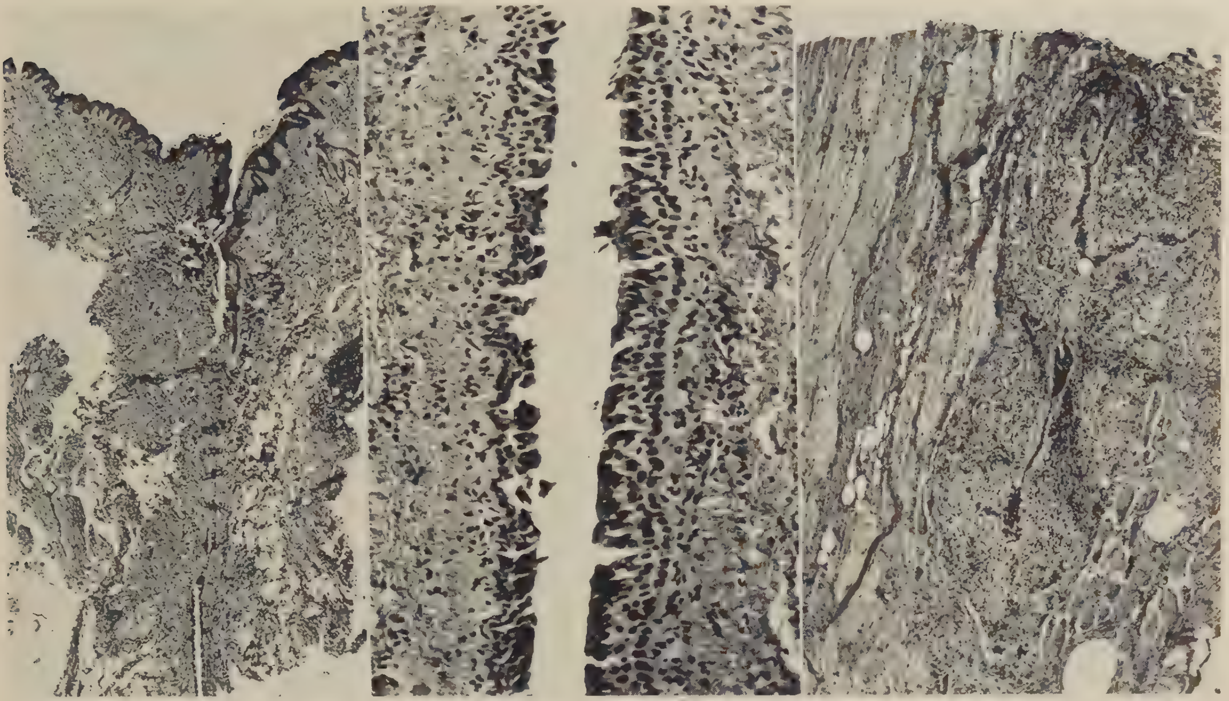
Multilocular cyst of more complicated type. x 10. Lining predominantly of lymphoepithelium. x 125. Dark foci are accumulations of lymph tissue, although it is said that a thyroglossal duct never contains lymphatic tissue. Associated fragments of thyroid and thymus glands are seen in detail, lower left.



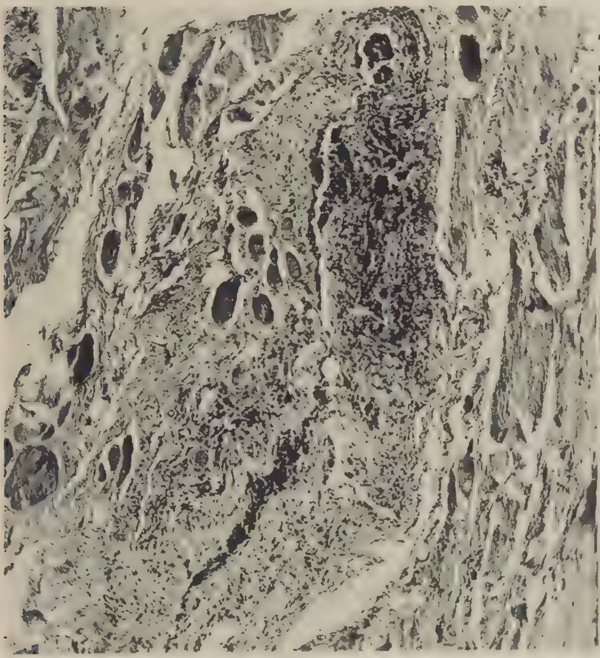
Colloid-containing thyroid acini and thymic tissue including a Hassall's corpuscle, from same cyst. x 75.



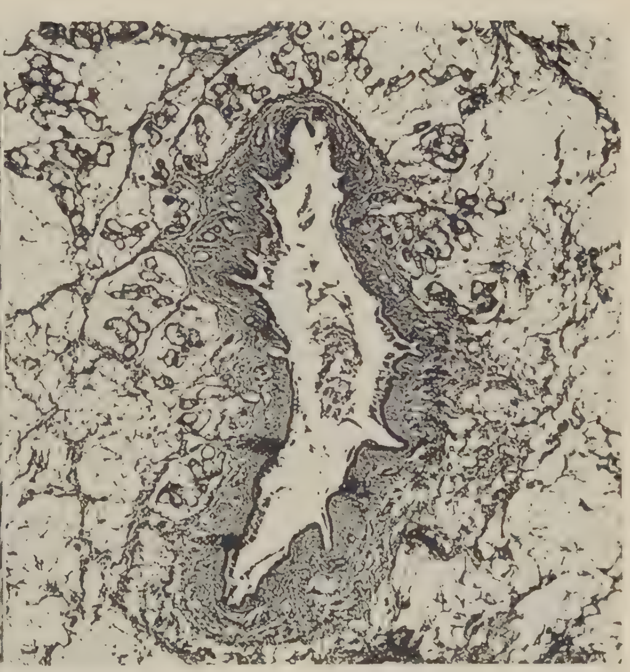
Fragment of persistent Reichert's cartilage in subcutaneous tissue of neck. No connection with cysts. x 10.



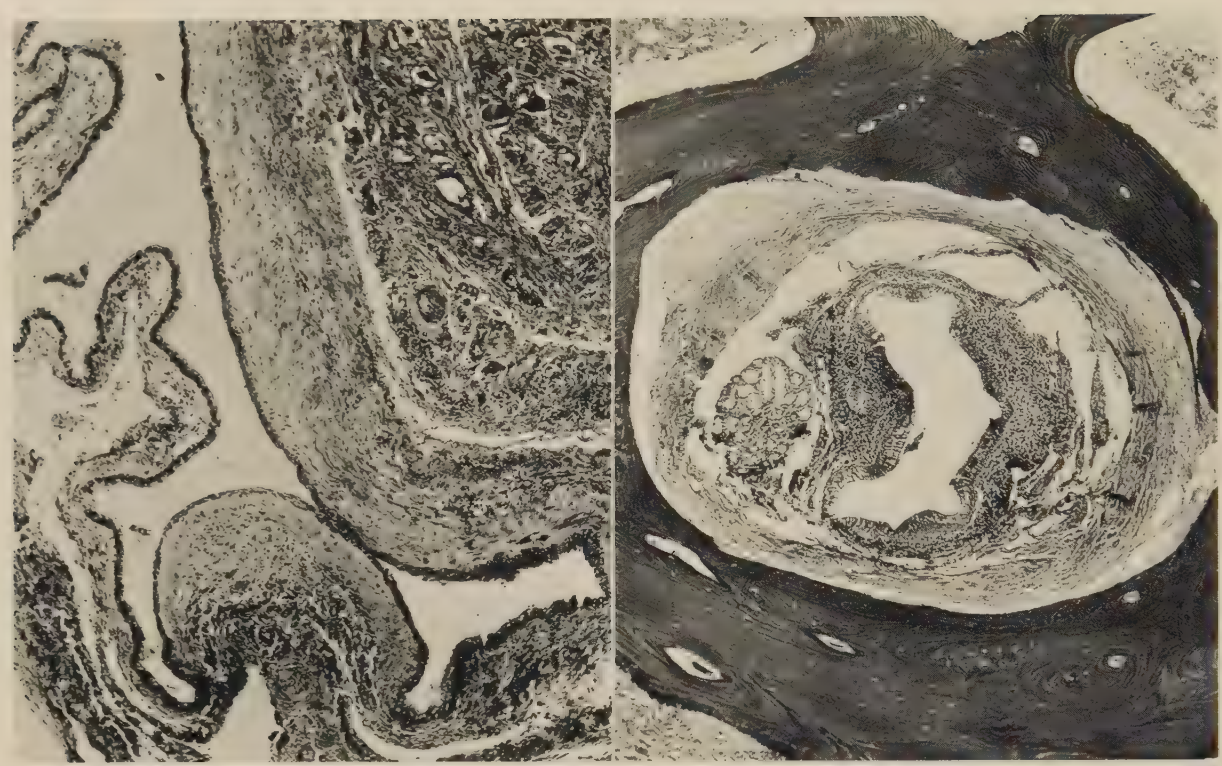
Lateral cervical (branchial) fistula. Draining sinus with cutaneous orifice over the anterior border of the sternocleidomastoid muscle below the hyoid bone, present since birth in 19 year old private. At operation the tract was easily followed, but appeared to end in a slip of muscle attached to the pharyngeal wall. *Left:* cutaneous orifice lined by squamous epithelium at top. The narrow lumen of the subcutaneous part of the tract can be seen at bottom. x15. *Center:* nonciliated respiratory-type epithelium of subcutaneous portion. x160. *Right:* mild chronic inflammatory reaction about deeper segment of tract, surrounded by muscle. x48.



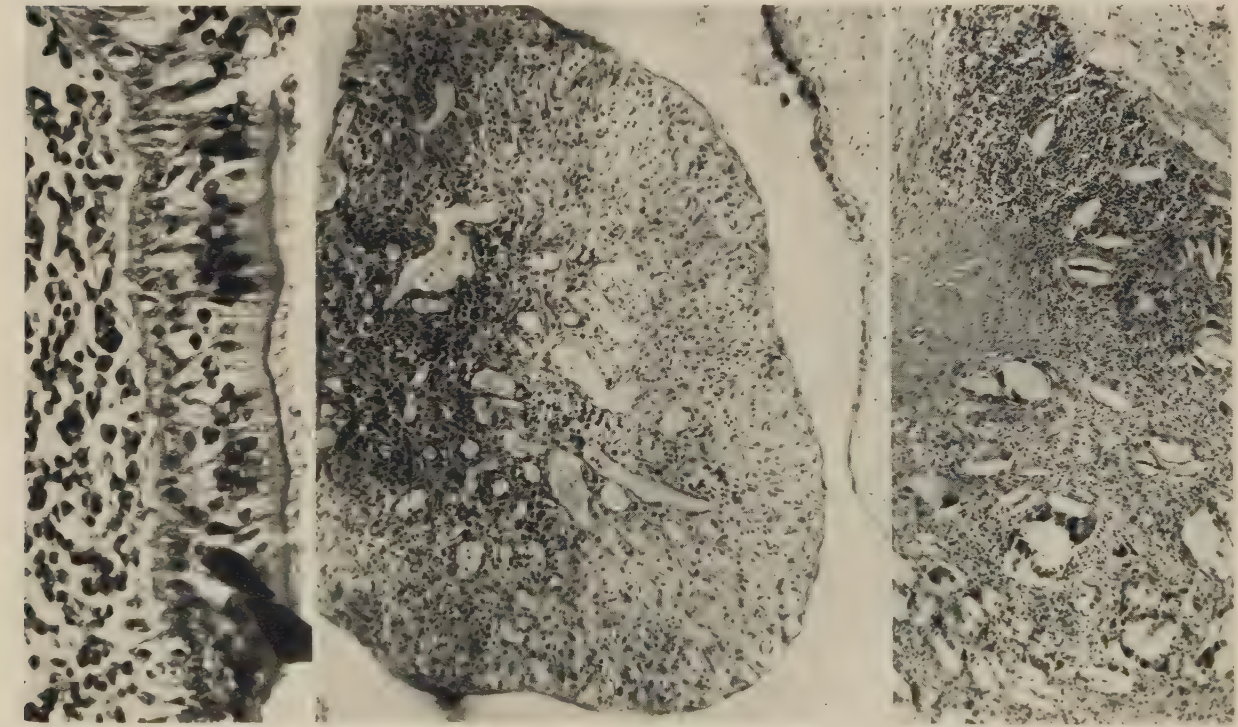
Pharyngeal end of fistulous tract near the tonsil had no grossly visible lumen; but was identified in numerous microscopic sections, one of which is shown. Slitlike, partly obliterated lumen; fibrous wall with dense chronic inflammatory exudate. x90.



Bronchogenic cyst, present since birth in "posterior shoulder region" of 1 year old baby. Preoperative diagnosis was cystic hygroma; submitting pathologic diagnosis, branchial cyst. Wall contains abundant smooth muscle, seromucinous glands; is lined by ciliated respiratory epithelium. x31.



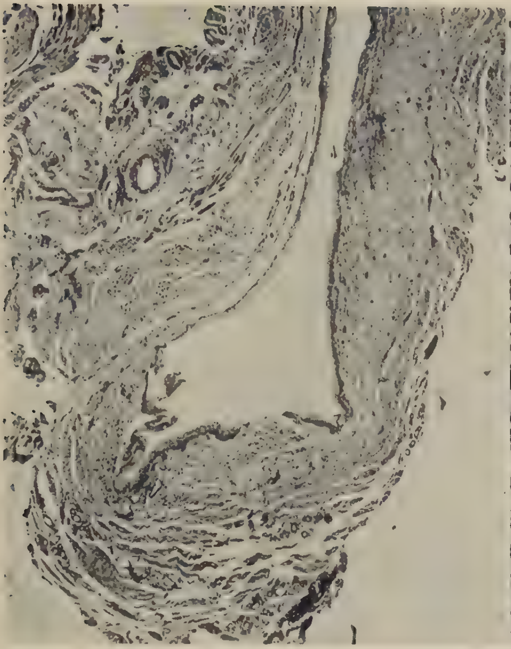
Midline cyst, generally unilocular. Those developing below the tongue are lined by ciliated pseudostratified epithelium and not the lymphoepithelium seen in some branchial cysts. The thyroglossal duct may persist through the hyoid bone, as at right. x 55, x 48.



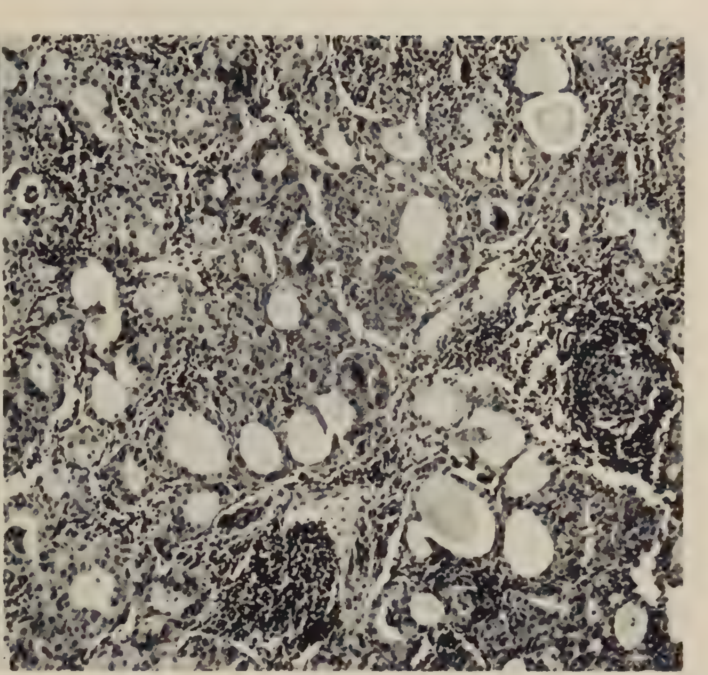
Detail of epithelium lining duct in hyoid bone *(left)*. x 400. "Hemangioma," resembling granuloma pyogenicum, projecting into cyst lumen *(center)*. x 100. Cholesterol slits in foreign body giant cells in an old hemorrhage *(right)*. x 150.

THYROGLOSSAL CYST

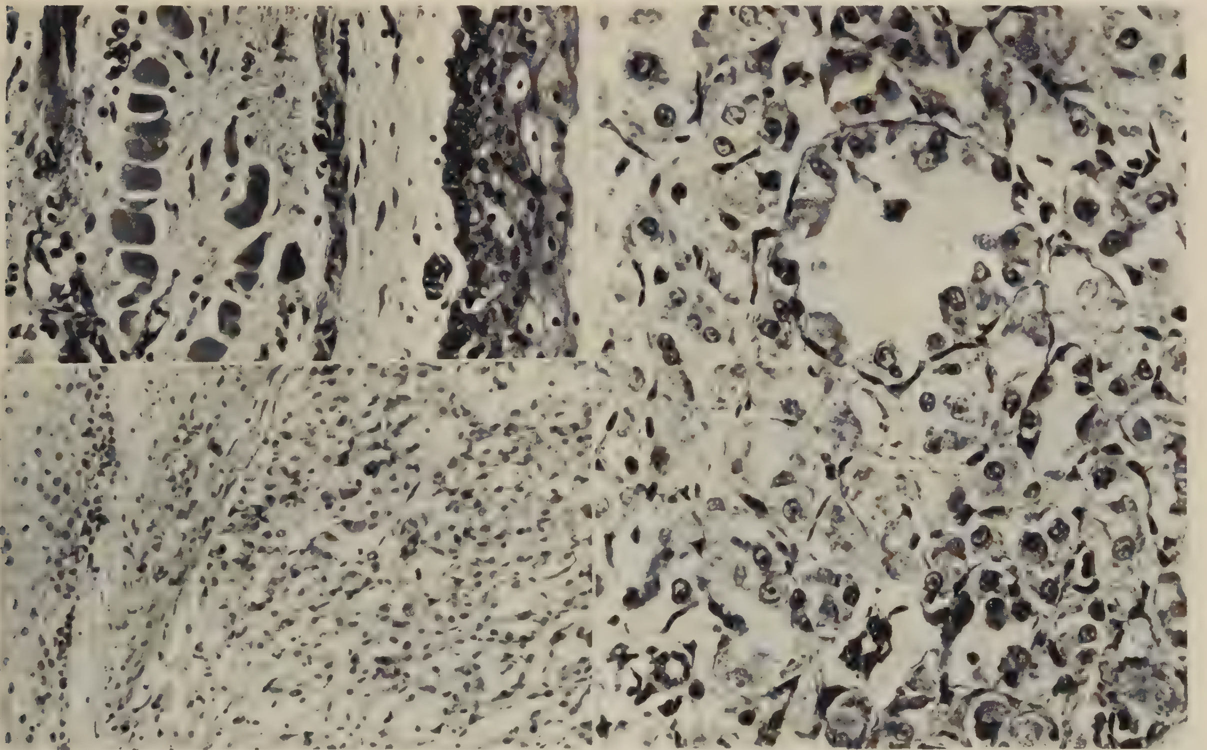
LINGUAL THYROID AND TUMOR



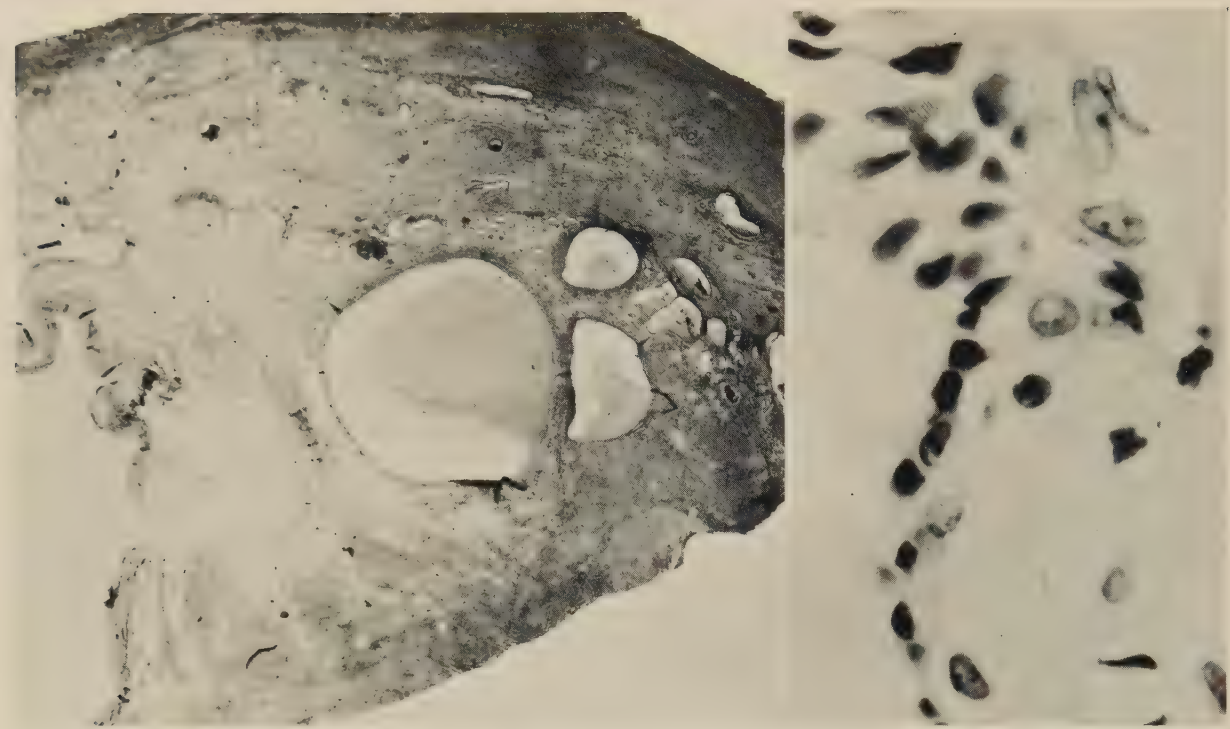
Thyroglossal cyst. Swelling at base of tongue, in infant two months of age. Milky fluid was aspirated, but cyst refilled. x 25. (S. S. Hall, Clarksburg, W. Va.)



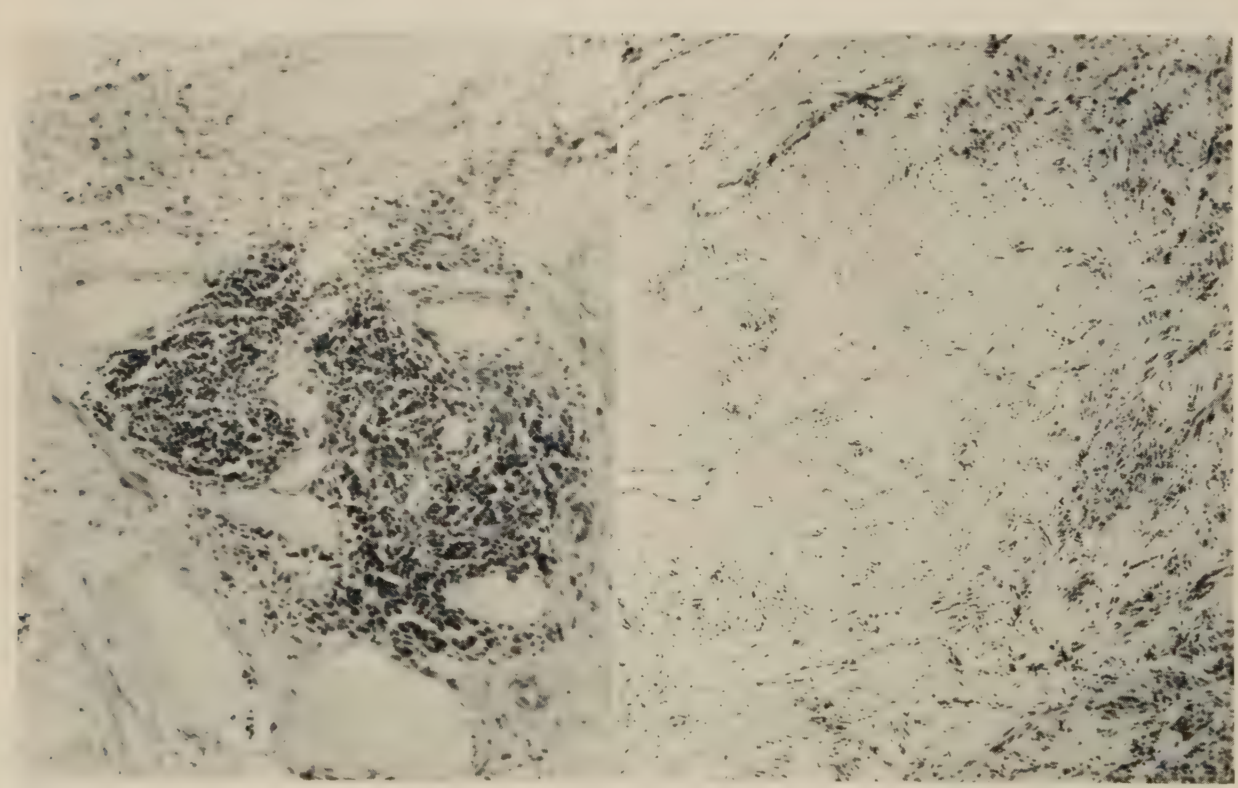
Lingual thyroid, from a 60 year old woman, with myxedema and a nodular thyroid. A firm mass at base of tongue interfered with swallowing. Hürthle type cells and lymphatic tissue contribute to a picture compatible with that of the Hashimoto thyroid. x 100.



A. **Squamous epithelial lining** with a few muscle fibers of tongue, from above left. x 280. B and C. **Embryonal carcinoma,** possibly from a thyroid rest. Mass in base of tongue of a 2 year old boy, who had not breathed properly since birth, pressed on epiglottis necessitating tracheotomy. Prompt recurrence after removal; death with metastasis in neck, six months later. At this low power the tumor looks encapsulated. x 100. Cell type and acinar arrangement suggest thyroid. x 300. (J. J. McLoone, Phoenix, Ariz.)



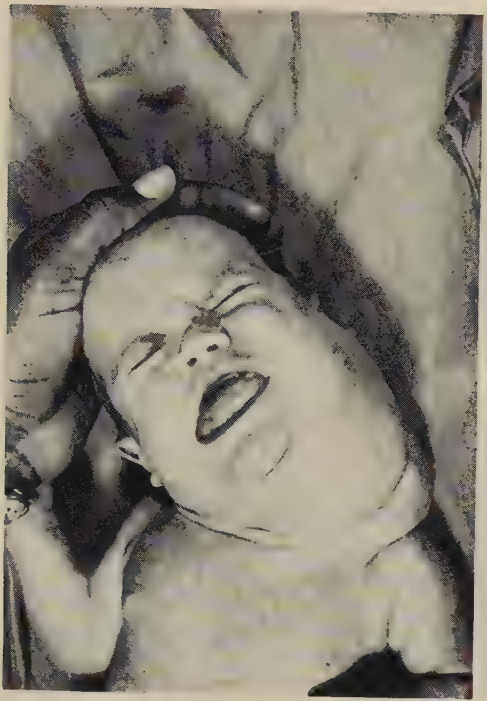
Mass, removed from a 42 year old man with a painless swelling of one year's duration, low on right side of neck. Generally dense tissue contains cysts of varying sizes. x 7. A single layer of endothelial cells lines the cysts. x 800.

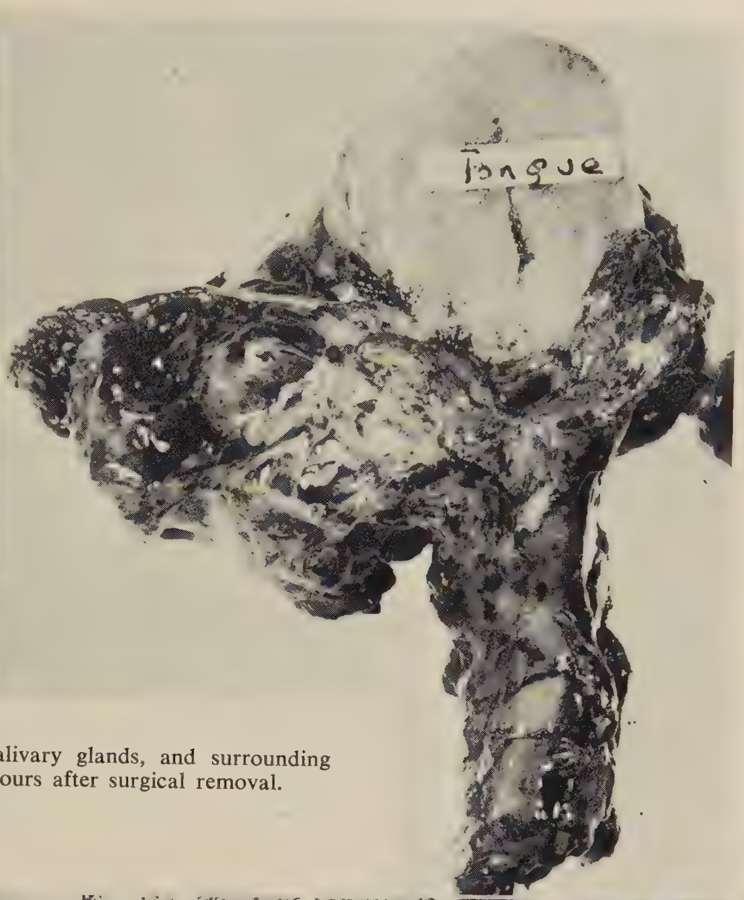


Other portions of the tumor are more cellular and here the vessels are smaller and more numerous. Areas of plasma cell infiltration indicate a chronic inflammatory reaction. x 140. Note the apparent growth activity of vessels. x 80.

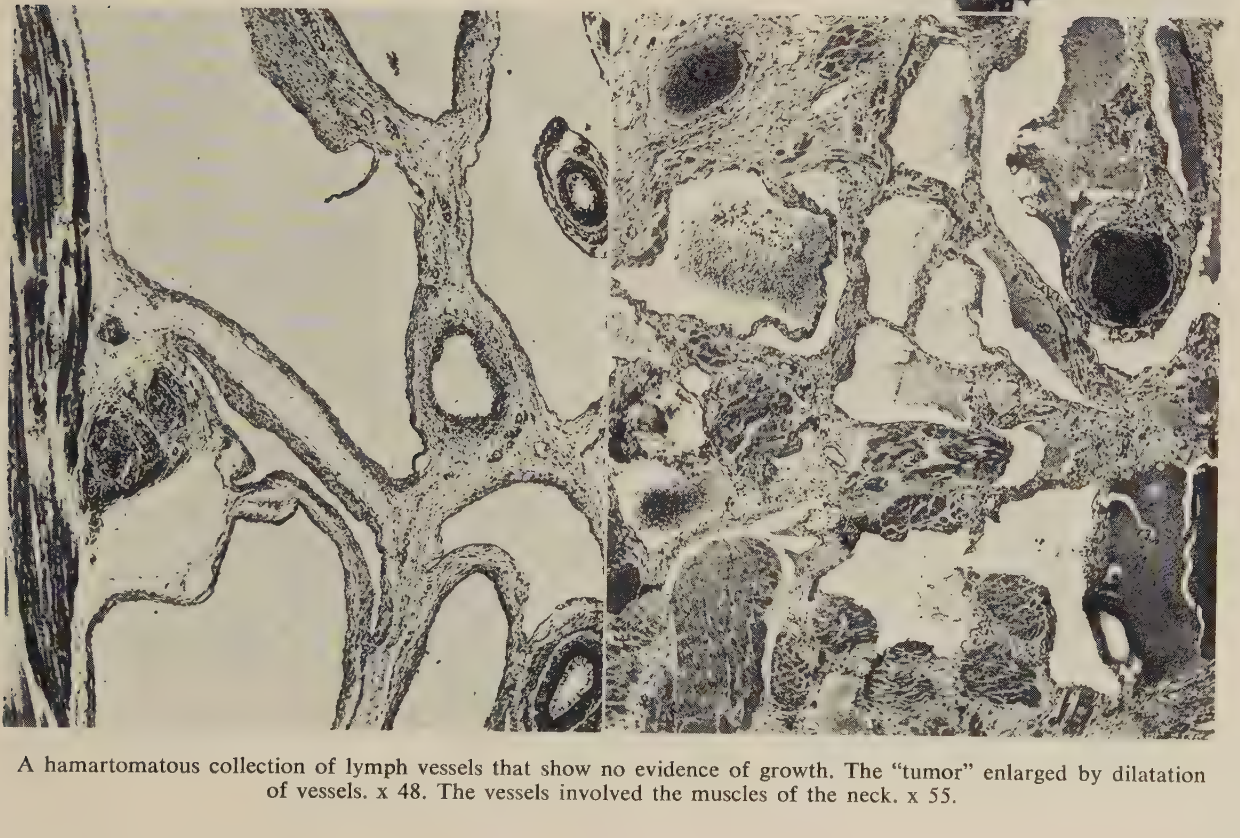
HYGROMA CYSTICUM COLLI

(CAVERNOUS LYMPHANGIOMA)





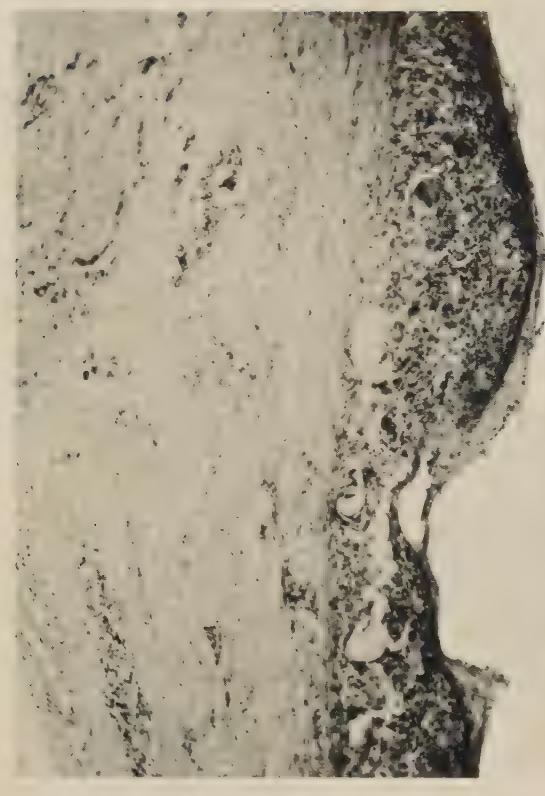
Congenital lesion, involving neck and all salivary glands, and surrounding trachea and larynx. Death occurred 48 hours after surgical removal.



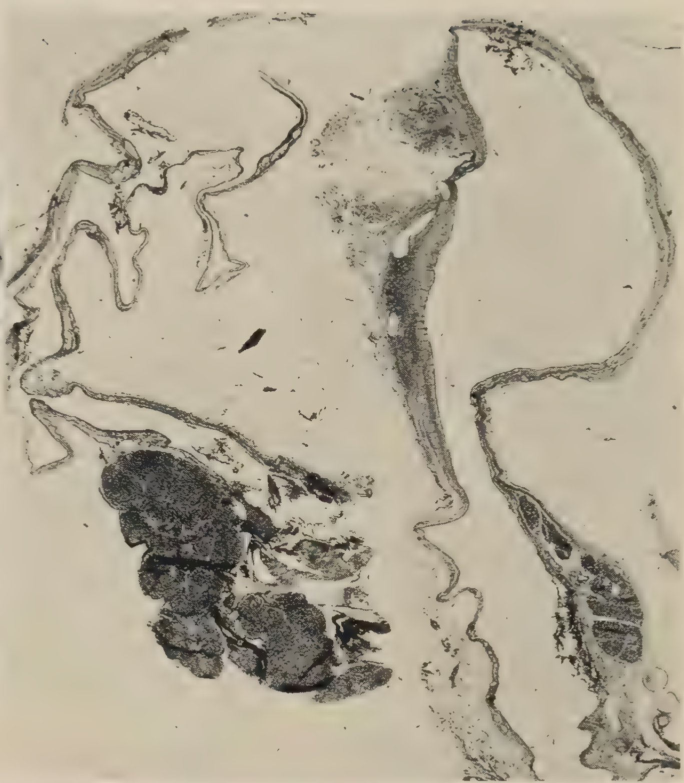
A hamartomatous collection of lymph vessels that show no evidence of growth. The "tumor" enlarged by dilatation of vessels. x 48. The vessels involved the muscles of the neck. x 55.

CYSTS OF NECK

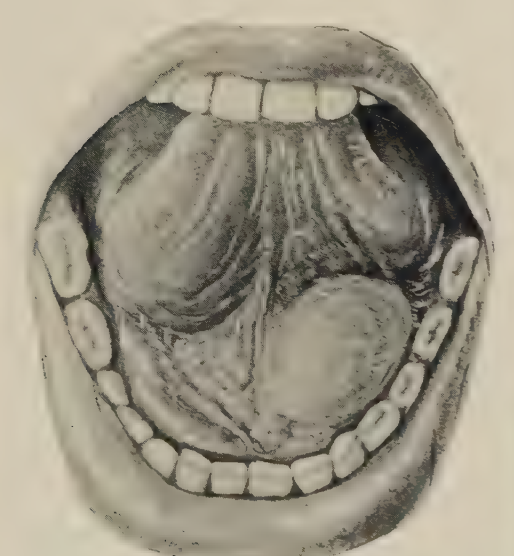
RANULA

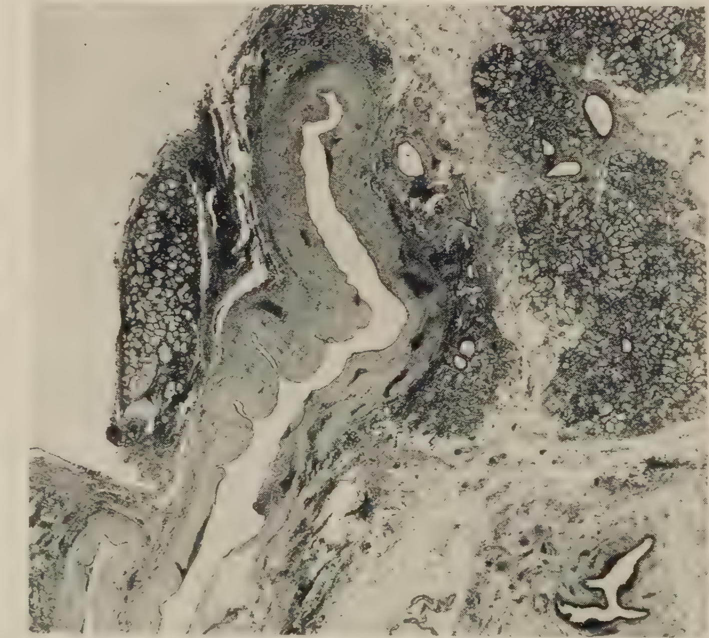


Dermoid cyst, to right of median line, adherent to skin but movable beneath. Frayed squamous epithelial lining; foreign body reaction in upper portion; several hairs in cross section. x60.

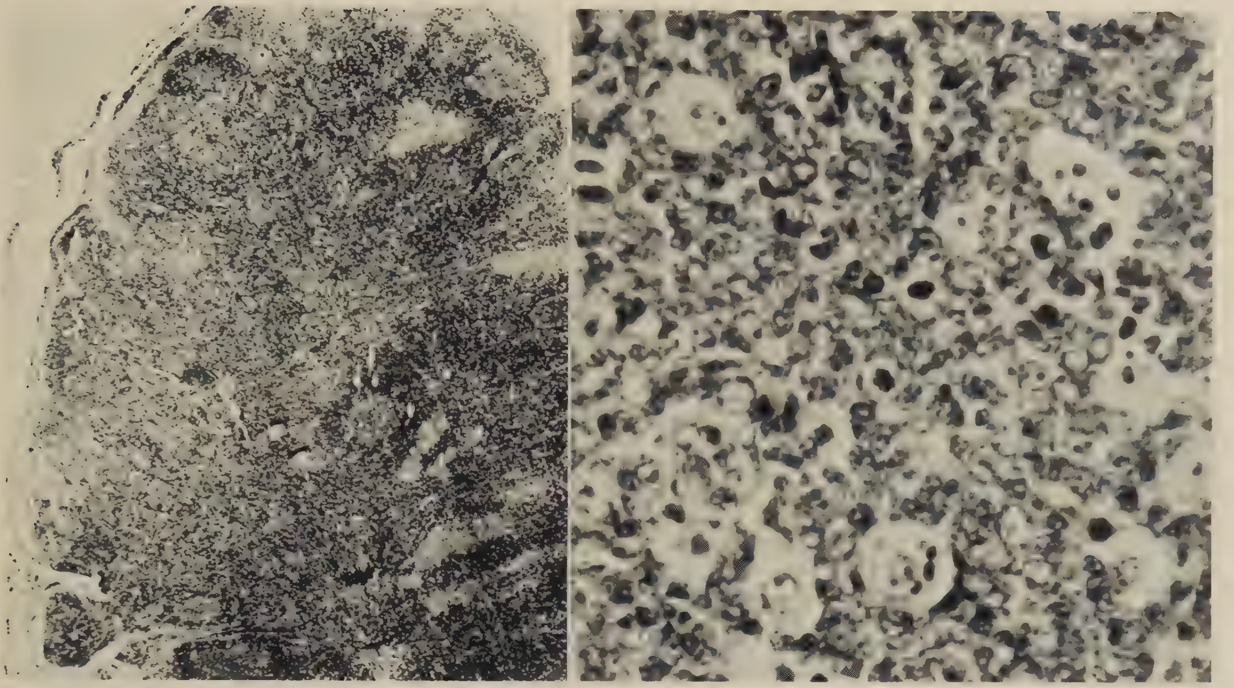


"Cystic" lymphangioma. Painless swelling of two months' duration below right angle of jaw of 22 year old man. "Cystic" structure is dilated lymphatic vessel lined by endothelium. Smaller lymphatic vessels and lobules of submaxillary gland in its wall. x7.

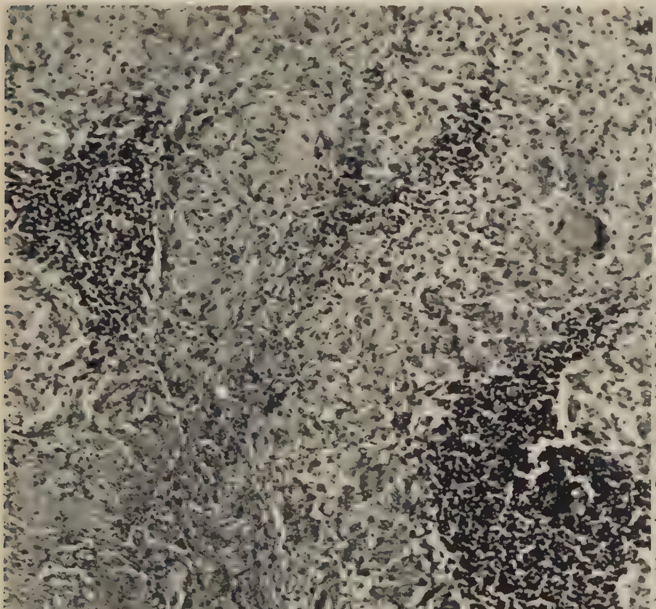




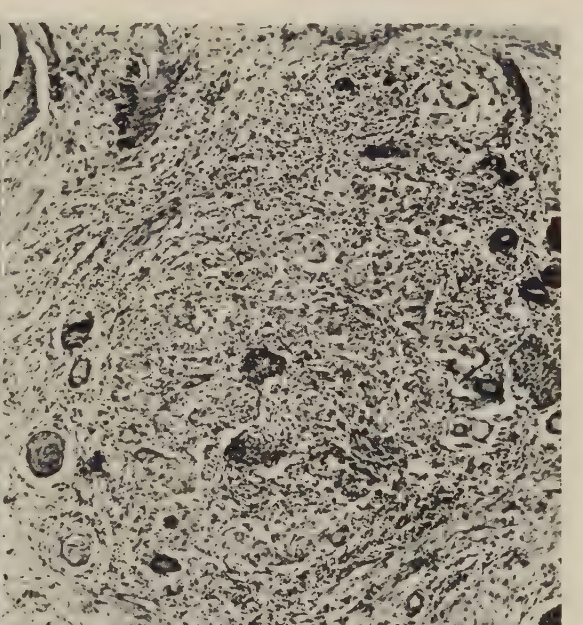
Ranula. A retention cyst in the floor of the mouth usually due to obstruction and dilatation of a duct of sublingual or submaxillary salivary glands *Left:* smooth, "bluish," unilateral ovoid swelling beneath tongue. *Right:* dilated duct, lined by cuboidal and flattened epithelial cells, is surrounded by atrophic lobules of sublingual salivary gland and adipose tissue. From 70 year old man. x30.



Reactive hyperplasia, nonspecific, of cervical lymph nodes is a common response to **nonspecific** regional inflammation and a not infrequent response to **specific** inflammatory conditions. The hyperplasia may primarily involve the follicles and their germinal centers, the sinusoids, or the medullary cords. Purulent exudate or chronic inflammatory exudate of plasma cells and macrophages that justify diagnoses of acute or chronic lymphadenitis respectively, may be inconspicuous or absent. *Left:* diffuse medullary hyperplasia obscuring sinusoids and follicles. x22. *Right:* hyperplastic reticulum cells, some in mitosis. Pronounced phagocytic activity indicates response to inflammation rather than neoplasia. x560.

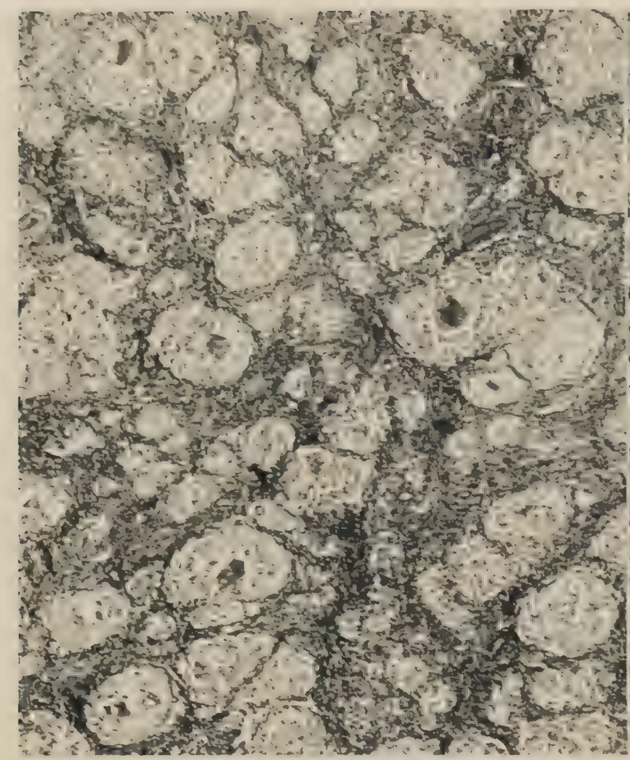


Tuberculosis of cervical lymph nodes. Occurs in disseminated tuberculosis, or from lymphatic drainage of primary site of infection such as tonsil or of secondarily involved structures of head and neck. Typical granulomas with central caseation necrosis.

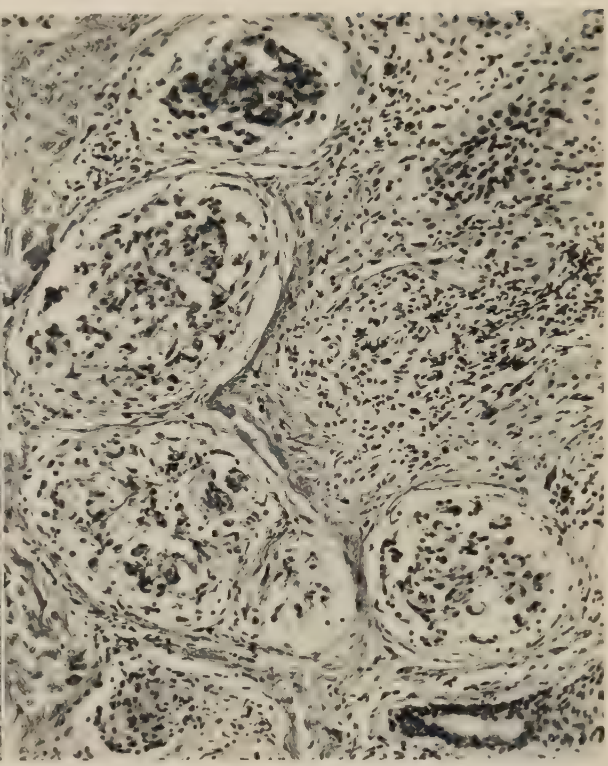


Scrofuloderma. Tuberculous nodules, ulcerations, and multiple sinuses of skin produced by direct extension from underlying involved structures. In the neck, almost always secondary to lymph node tuberculosis. x90.

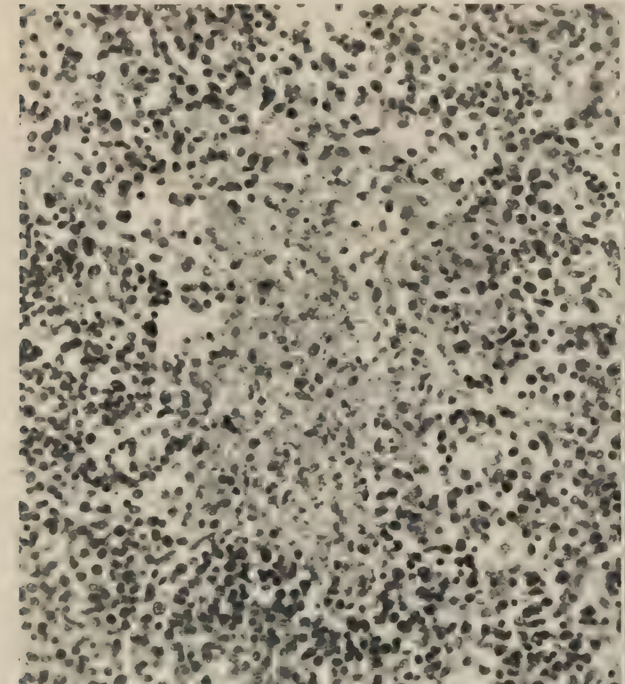
GRANULOMAS



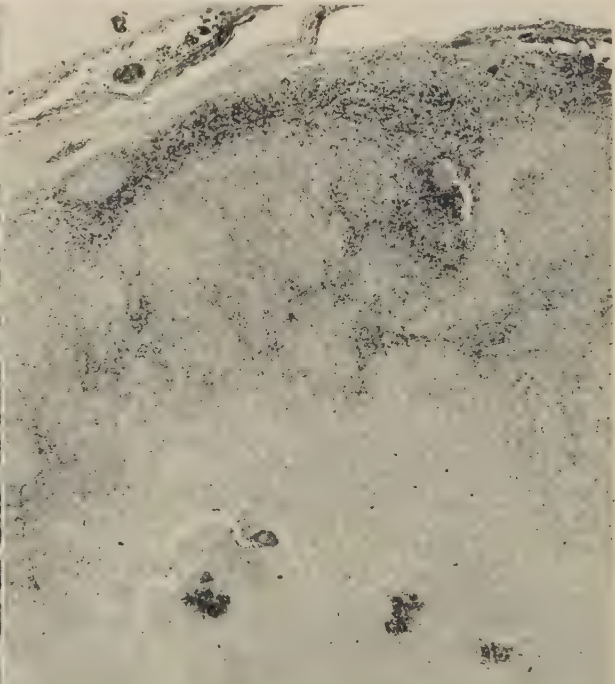
Boeck's sarcoid is characterized by discrete, non-necrotic tubercles, sharply outlined, but the diagnosis cannot be made without complete history.



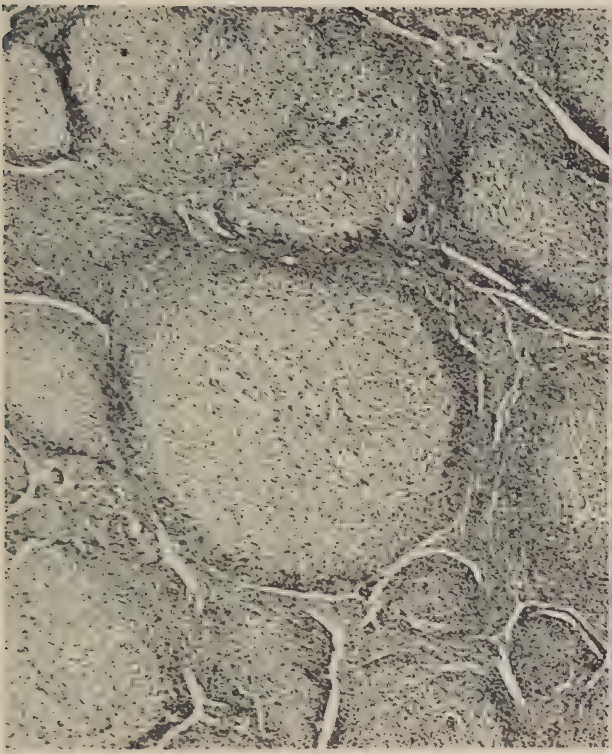
Questionable sarcoid, in skin of ear of a child. Sharply circumscribed tubercules in fibrosed dermis. Foreign body reaction is also a possibility. x 120.



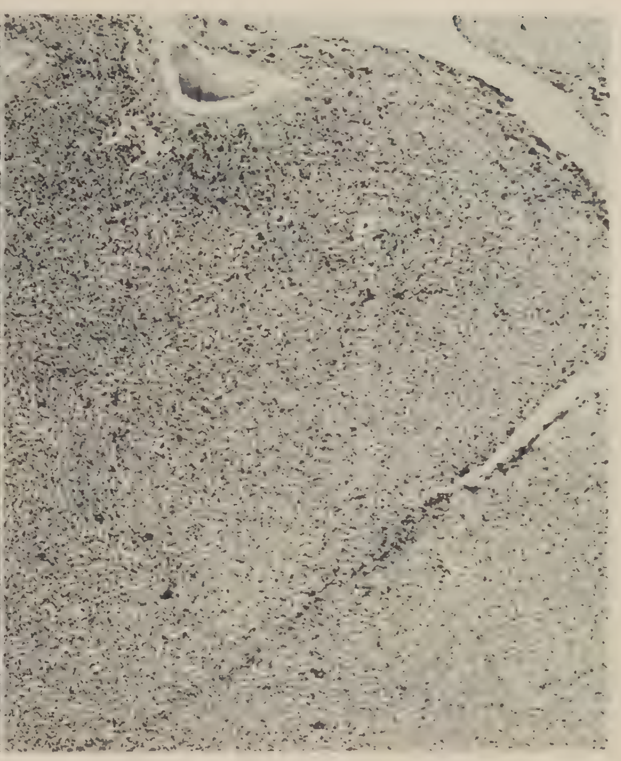
Tularemia, cervical node. Instead of the usually stellate tubercle it is seen here as a less well defined epithelioid reaction with necrosis. x 275.



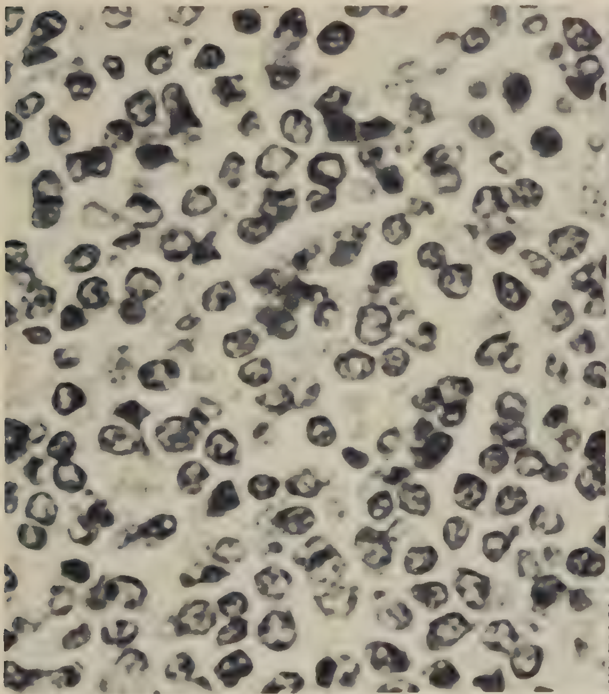
Actinomycosis (?), cervical node. Gland largely replaced by tubercles in which there are abscesses containing fungus colonies resembling Actinomyces. x 30.



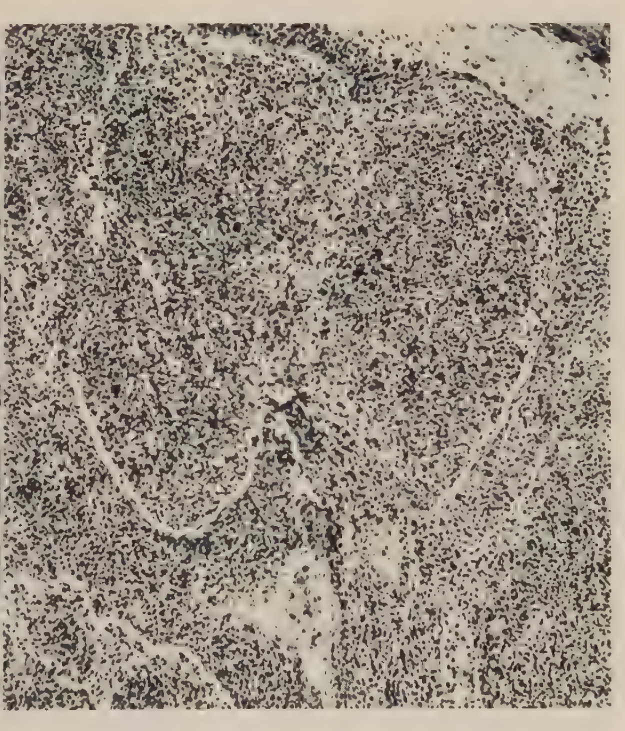
Giant follicular lymphoblastoma (Brill-Symmers disease) is characterized by increase in number and size of follicles. It frequently precedes by years a malignant lymphoma.



Lymphosarcoma obliterates the node architecture by neoplastic proliferation of lymphocytes. The latter also infiltrate the capsule (at top).



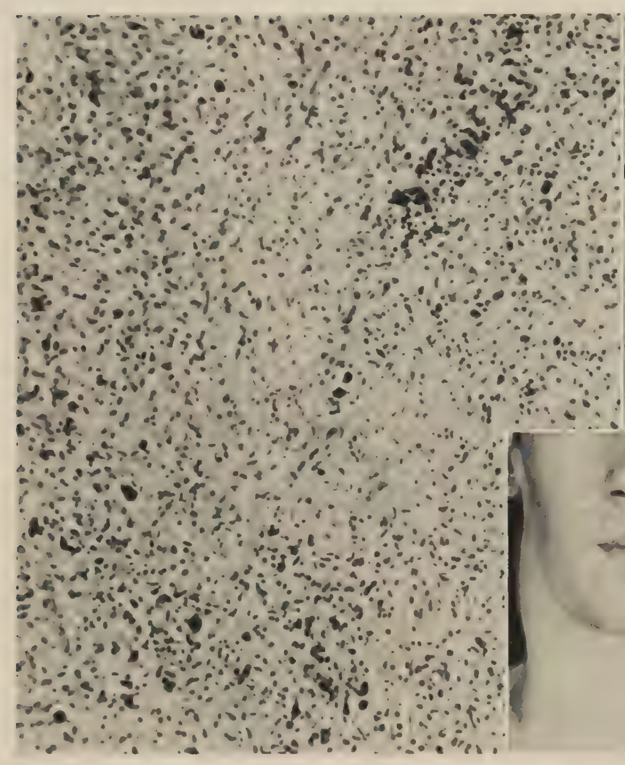
Neoplastic character of cells of lymphosarcoma. x 700.



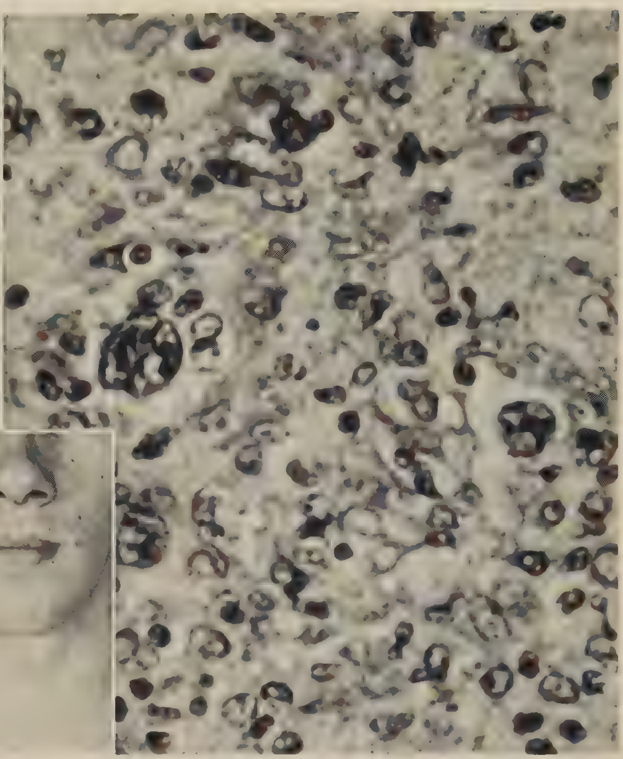
Acute monocytic leukemia. In lymp nodes, infiltration of leukemic cells produces a picture similar to that of lymphosarcoma. Differentiation depends on the blood picture. x 75.

CERVICAL LYMPH NODES

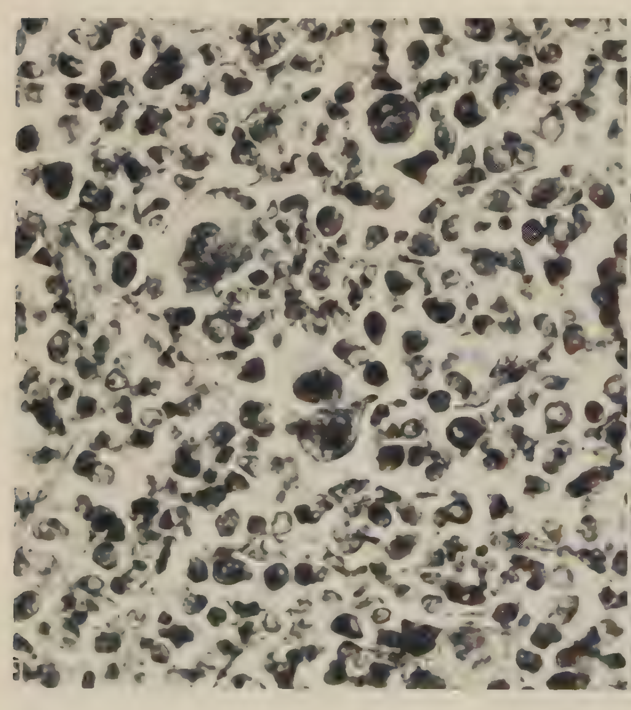
HODGKIN'S DISEASE



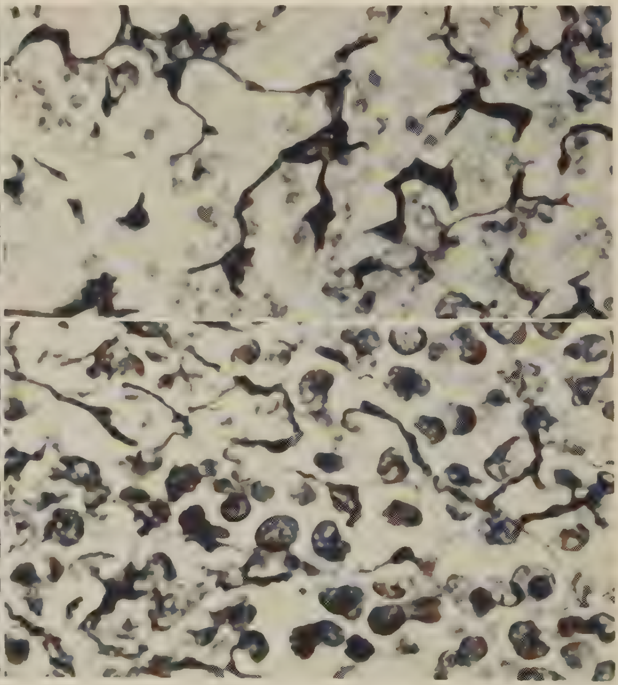
Diffuse sarcomatous involvement of lymph nodes. The dark spots are Reed-Sternberg cells. x 150. Inset: swollen cervical lymph nodes, the primary clinical manifestations of Hodgkin's disease.



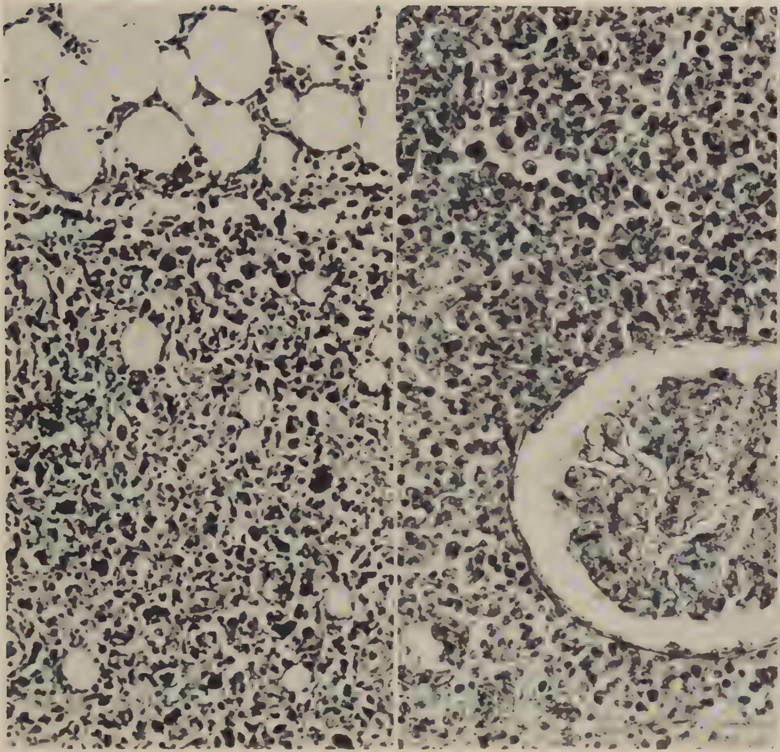
Scattered large mononucleated and multinucleated cells in a background of atypical reticuloendothelial cells. x 680.



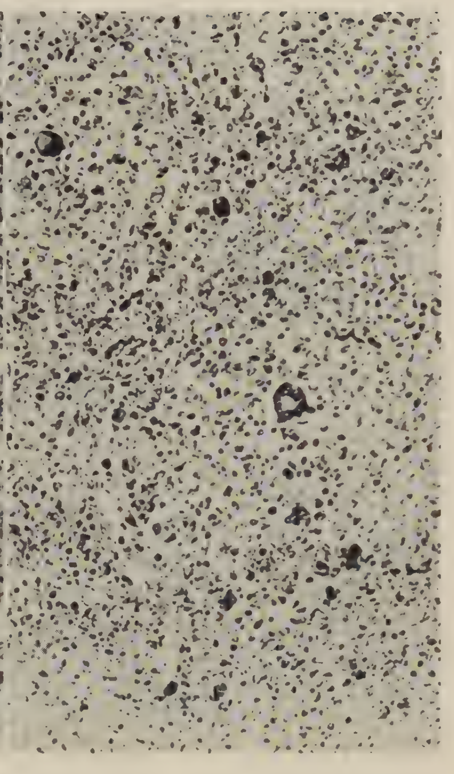
The same histologic picture, including a more typical binucleated Reed-Sternberg cell, in tissue obtained at autopsy. x 594.



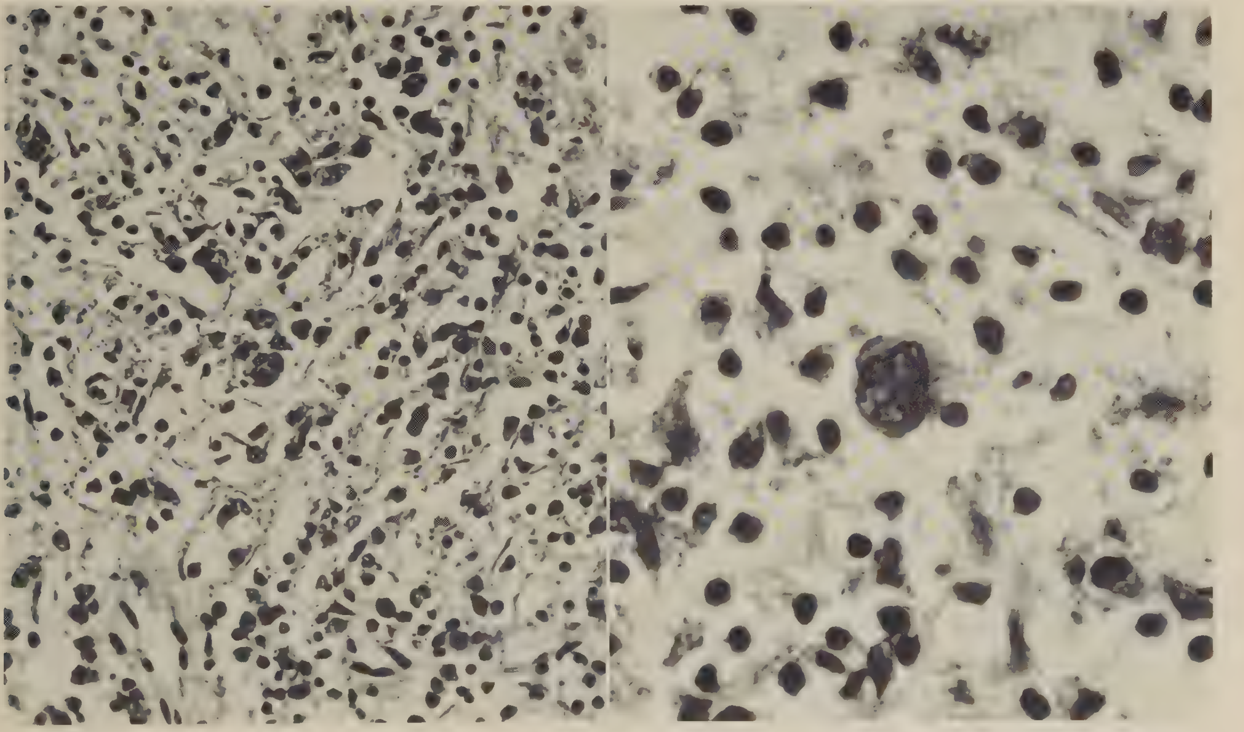
The "broken-twig" type of reticulin seen in Hodgkin's disease *(upper)* in contrast with the more delicate fibrils associated with individual cells in reticulum-cell sarcoma *(lower)*. x 915, x 475.



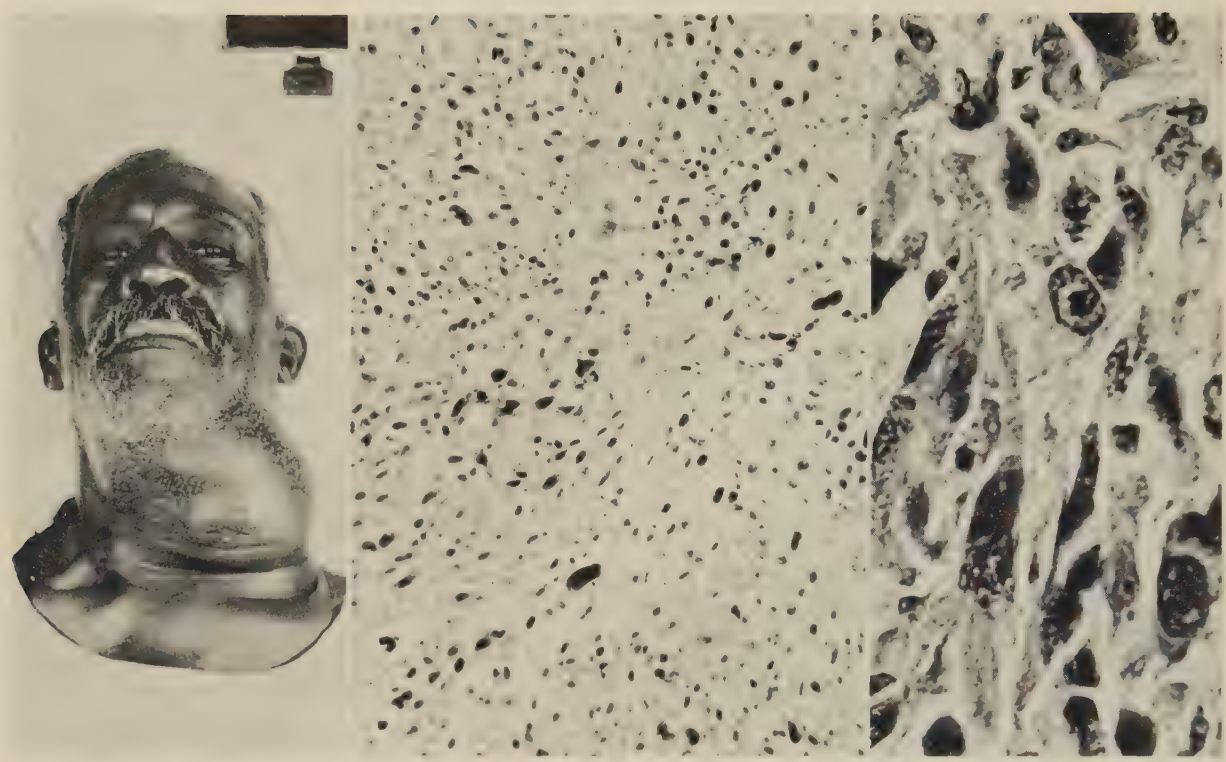
Tumor cells have invaded the fat surrounding the involved lymph node (x 135) and also have metastasized to the kidney. A glomerulus identifies the latter. x 260. Typical of the generalized sarcomatous spread that may be terminal phase of Hodgkin's disease.



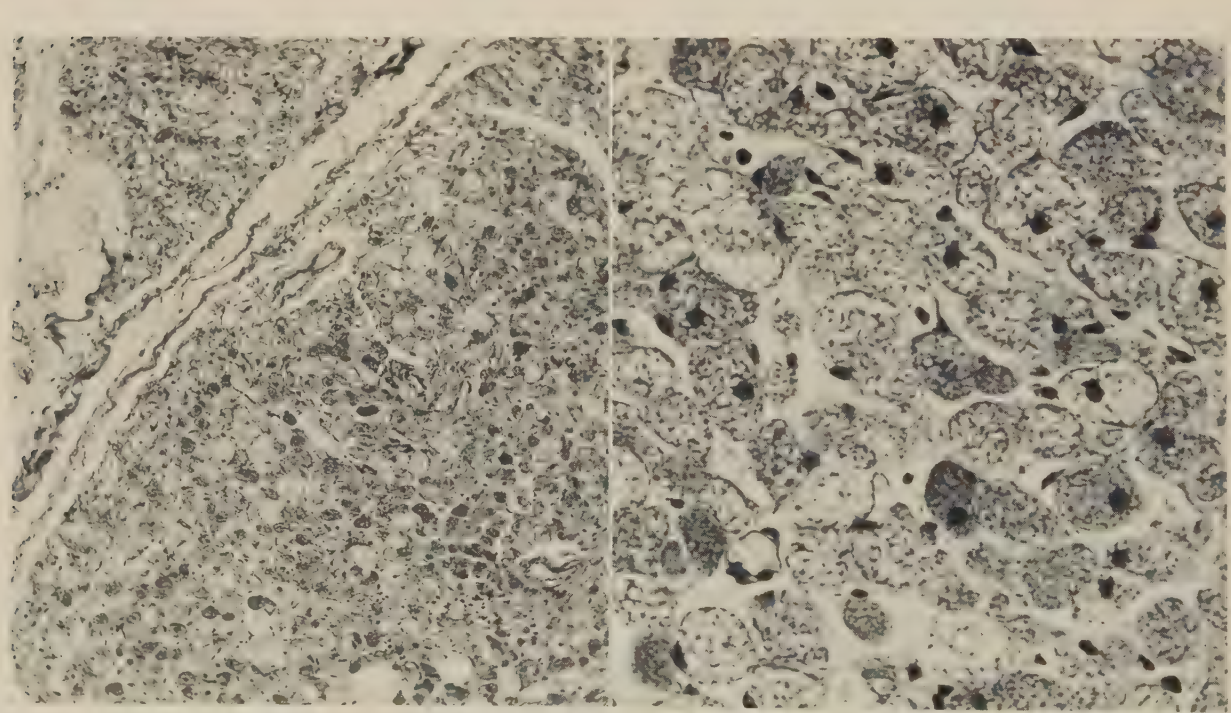
Brucellosis, spleen, producing a picture superficially resembling Hodgkin's disease.



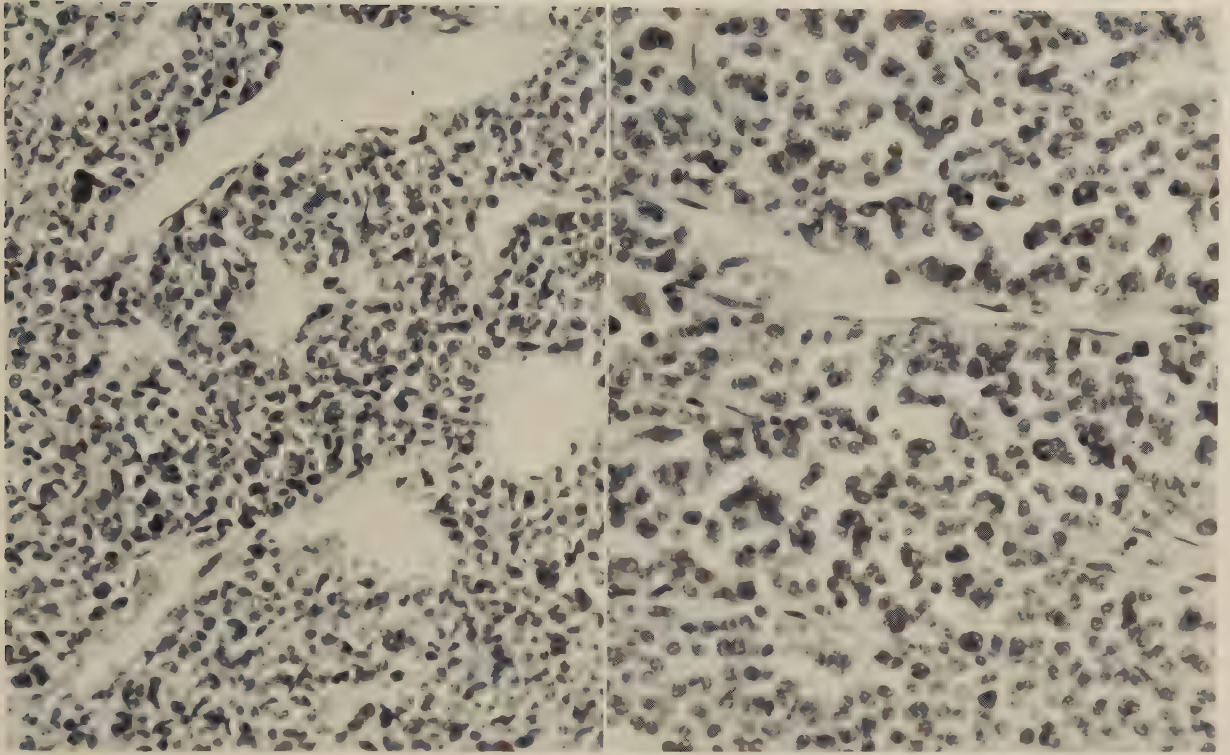
Hodgkin's disease of lymph node after treatment with nitrogen mustard. Reduction in number of tumor cells and an increase in stroma. x 330. Atypical cells are still present, but there are more normal lymphocytes. x 900.



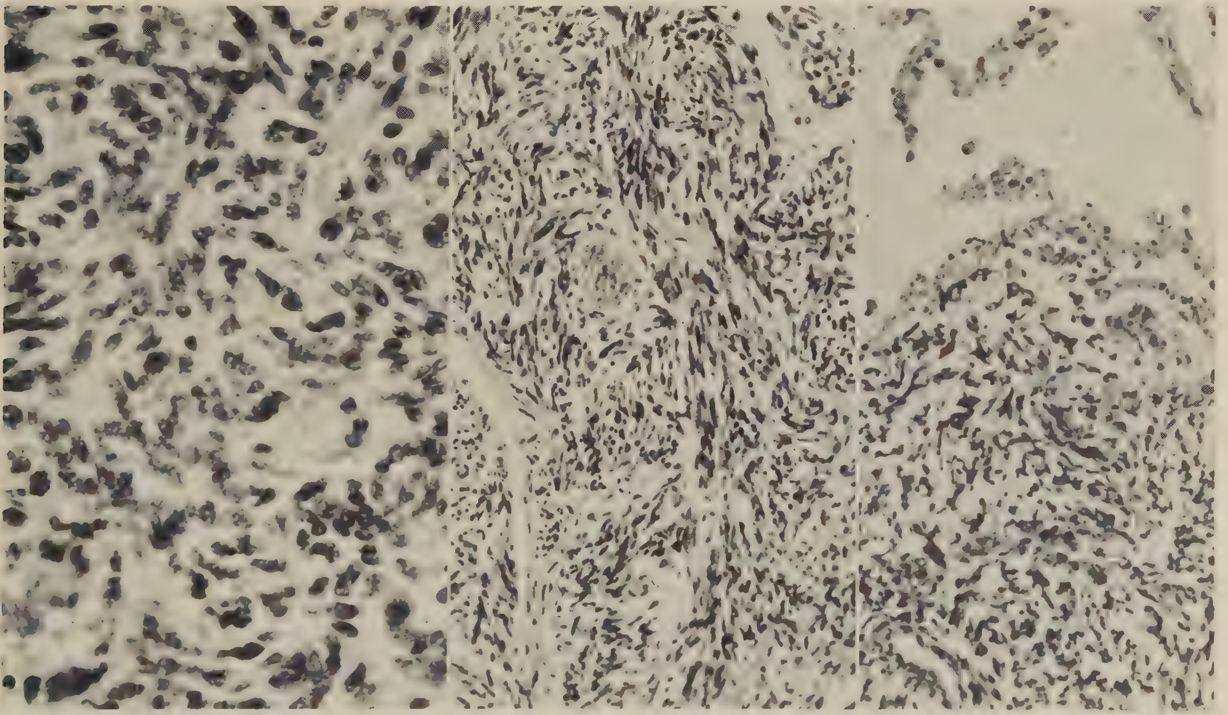
Rhabdomyosarcoma. Extensive invasion prevented recognition of the exact site of origin of this tumor, which eventually compromised the trachea and great vessels, but did not metastasize. The characteristic pleomorphism is seen at this magnification. x350. The ribbony cytoplasm, bizarre nuclei and suggestion of striations are diagnostic. x800.



Hibernoma ("brown fat tumor"), a rare benign subcutaneous tumor that resembles the hibernating organs of some animals. Lobules of prominently vacuolated, lipid-filled cells with small nuclei. Such cells are readily distinguished from those of ordinary fat and should not be confused with the cells in granular cell myoblastoma or with xanthoma cells. x75, x330. Reports have included neck, back, axilla, thigh and mediastinum as sites of origin. (A.P. Stout, N.Y.)

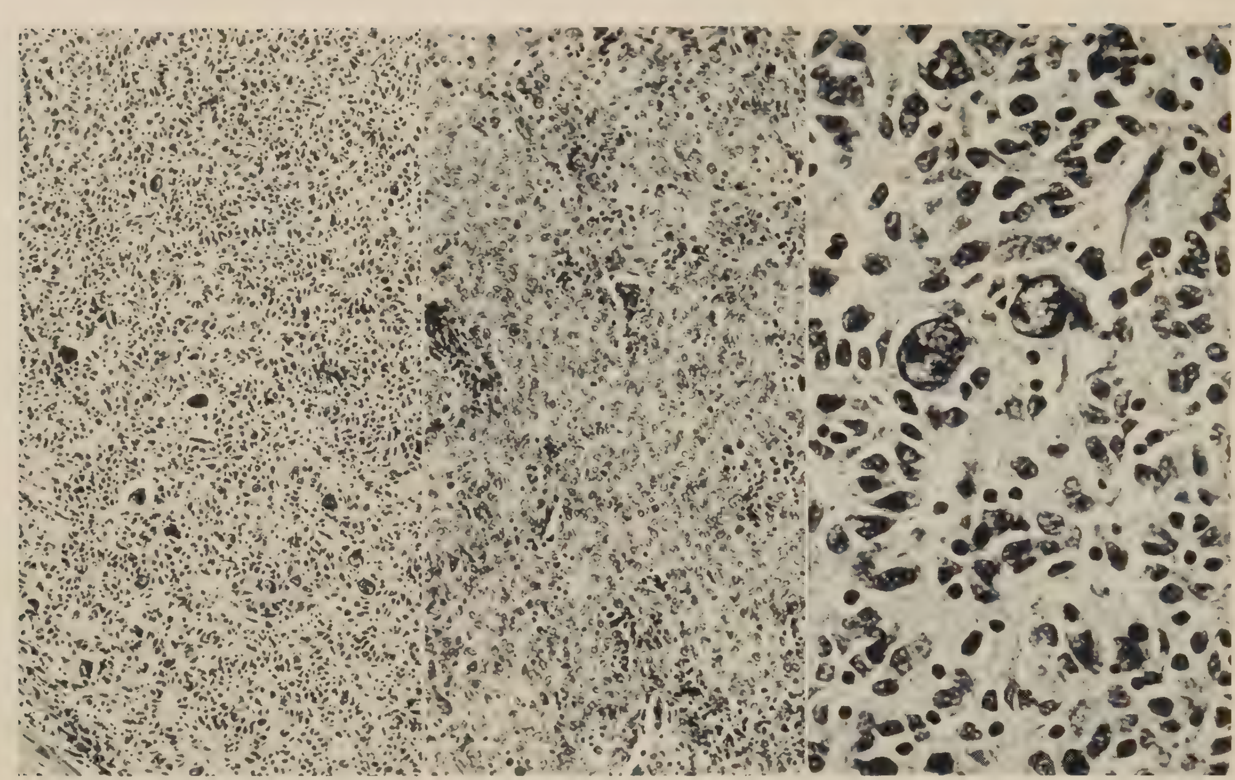


Neurogenic sarcoma, recurrent tumor involving cervicobrachial plexus of a 28 year old Negro. Irradiation therapy was ineffectual and he died with lung metastasis. Primitive cells suggesting neuroblasts have an intimate relation to endothelial lined channels. x 310, x 395.

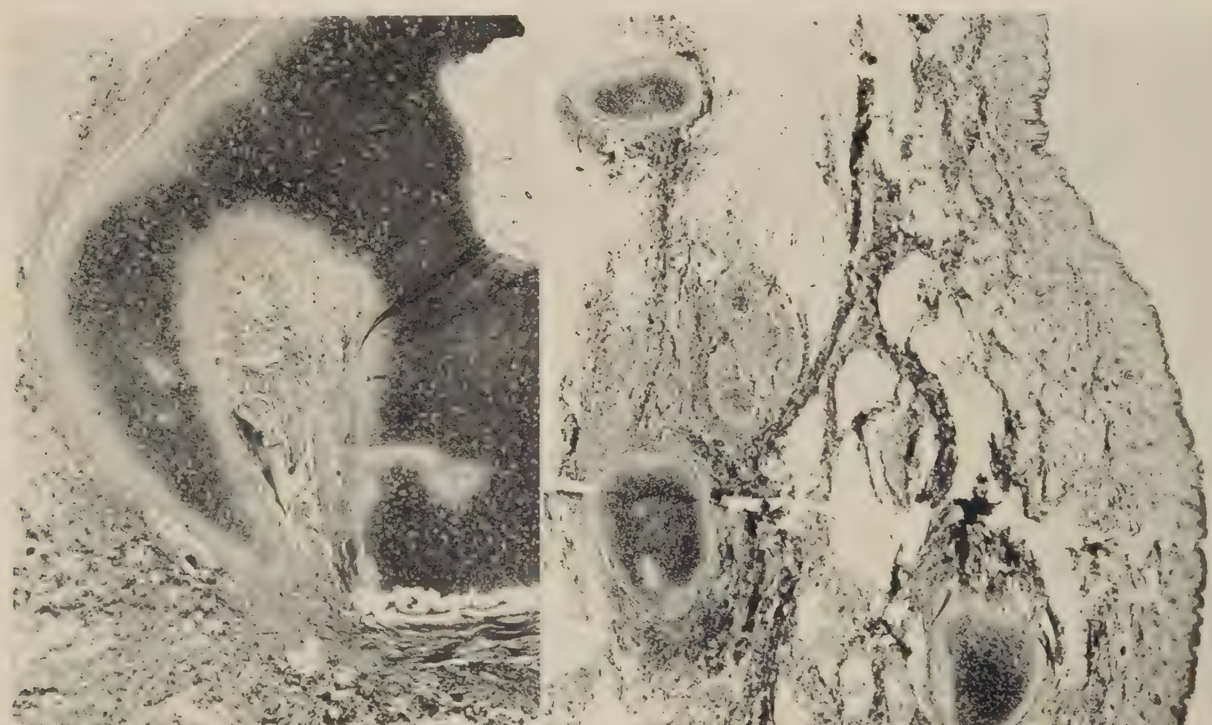


Tumor, cervicobrachial plexus, from a 33 year old man. It began as a paravertebral mass in the back of the neck, diagnosed sarcoma. Death four years later was due to extensive involvement of spinal cord. The cells of this tumor are spindle shaped. The cell borders are indistinct and a suggestion of rosette arrangement is seen *(left).* x 450. "Nuclear regimentation" rather than the palisading seen in neurilemoma *(center).* x 160. Metastasis to lung *(right).* x 160.

(Case 6 and Case 7 from Primary Malignant Tumor of Nerve, by I. Gore, Cancer 5:278-296, 1952.)



Tumor, submandibular tissue, in a 16 year old girl. First appeared as small mass that was drained. Pathologic diagnoses of peripheral ganglioneuroma, malignant melanoma, and undifferentiated carcinoma, and one and a half years later of Hodgkin's disease. X-ray treatment and radical neck dissection eradicated tumor from mouth, pharynx, nasopharynx. Tumor appears epithelial, but bizarre. x 100, x 135, x 395.



Remnants of Reichert's cartilage in subcutaneous tissue of neck of a 22 year old man. Present since birth, its growth was in proportion to that of the patient. Such remnants may persist anywhere along embryonal course of the cartilage from styloid to hyoid. Well differentiated cartilage in close proximity to skin. x 23, x 9.

CHAPTER 29

THYROID AND PARATHYROID GLANDS AND CAROTID BODY

THYROID GLANDS

The thyroid gland is a downgrowth from the primitive pharynx. Developing as a mass in the base of the tongue, it invaginates downward as a tube, the thyroglossal duct. The gland forms rapidly in its permanent site, and normally the duct becomes obliterated early in fetal life. The site of origin in the tongue is marked by the foramen caecum. Residua of thyroid tissue may be encountered anywhere along the course of the original duct, including the base of the tongue. An example of what is interpreted as a tumor arising in this embryonal thyroid anlage in the base of the tongue is included in the following illustrations.

If the tube fails to close in any part of its course, a sinus opening may result at the site of the foramen caecum in the base of the tongue and extend for varying depths into the neck in front of the trachea. If this opening is obliterated and a lumen remains below, the result is the clinical **thyroglossal cyst.** Such cysts are manifest clinically in the midline, a location which differentiates them from branchial cysts which develop laterally. Since the original thyroglossal duct passes through the hyoid bone, a thyroglossal cyst may involve this same structure.

Histologically, cysts which arise in the upper segment of the thyroglossal duct are usually lined by squamous epithelium which may present intimately associated lymphatic elements. Cysts of the lower segment of the duct are usually lined by the respiratory type of epithelium. Fragments of thyroid tissue are a common component in the subepithelial tissue and are present as characteristic acini lined by low cuboidal epithelium and containing colloid. Another feature is a mass of hemangiomatous tissue which may project into the lumen of the cyst.

If such cysts become infected, the lining epithelium may be lost and replaced by granulation tissue. Occasionally these infections point to the surface of the neck and result in a chronic discharging sinus, usually in the midline, but at times just to the side of it.

For our purposes it is not necessary to go into the details of the pathology of the thyroid gland. Much of it is still controversial, but there are several entities with which the otolaryngologist should be familiar. Among the most controversial are the inflammatory lesions.

Struma Lymphomatosa (Hashimoto's Disease).— Clinically the condition manifests itself by uniform enlargement of the gland. If there is any clinical evidence of functional disturbance it is of hypothyroidism. Pressure on the trachea causes the chief objective symptoms. The condition is more frequent in women and those in adult life.

Grossly, the gland is uniformly enlarged and may be two or three times its normal size. The capsule is intact and nonadherent to the surrounding structures. No normal thyroid tissue or colloid can be recognized on the cut surface.

Histologically, diffuse infiltration of the thyroid gland by lymphoid cells is associated with decrease in the glandular parenchyma. The epithelium loses much of its acinar arrangement and appears as clusters of cells surrounded by the lymphoid element. Well defined secondary lymphatic follicles are always present, and, although considered by some to occur only in this disease, they may also be found in toxic goiters and other conditions. There is a varying degree of fibrosis of the gland stroma.

The nature of the condition is not understood. It is not really an inflammatory reaction and is more likely on a metabolic or retrogressive basis.

Riedel's struma may at times be difficult to distinguish from Hashimoto's disease and is considered by some to be the end stage of the latter. It is, however, more frequent in men. The gland is much smaller and more firmly fixed than in Hashimoto's disease, and the fibrosis extends into the surrounding tissues. In spite of its small size, it causes more constriction of the trachea because it is adherent to this structure and the connective tissue of the fibrous process tends to contract.

Microscopically, fibrosis is marked and there is much destruction of the gland elements. Lymphocytic infiltration is diffuse, but secondary lymphatic follicles are not as common as in the Hashimoto thyroid. Other differences in the histologic picture are the abundance of giant cells and formation of pseudotubercles. The formation of these structures is stimulated by colloid material released from the destroyed acini. It is not uncommon for such pseudotubercles to be misinterpreted as tuberculosis.

As clear-cut as the two histologic entities may seem, it is now recognized that there is a group of inflammatory conditions that do not conform to either picture. The new category is **subacute thyroiditis** that seems to run a more benign course than the

Hashimoto or Riedel diseases. De Quervain first recognized the condition. These patients do not have a history of previous thyroid difficulty, but following a febrile and constitutional reaction, especially involving the throat and ear, pain in the thyroid is experienced and the gland becomes enlarged and tender. On removal the gland is hard. Microscopically, there is dense and diffuse fibrosis, destruction of the gland acini, focal cellular exudate including polymorphonuclear leukocytes, and, characteristically, foreign body tubercles like those seen in Riedel's struma. The difference between the two seems to be in the more cellular, definitely inflammatory reaction, the spottier distribution of the changes, and especially the absence of involvement of the surrounding tissue in subacute thyroiditis. Clinically, the subacute form appears to be self-limiting and not the progressively constricting process of Riedel's struma. Irradiation therapy seems preferable to surgical measures. Crile and Rumsey have recently summarized their experience with the disease.

Bacterial infections of the thyroid are rare, and tuberculosis particularly so. The gland may be the seat of gumma in the tertiary stage of syphilis.

Goiter.—From a clinical standpoint the changes in the thyroid parenchyma may be divided on the basis of hormonal activity into (1) toxic hyperthyroidism, (2) non-toxic hypertrophy, and (3) myxedema (hypothyroidism).

Pathologically, goiter or struma may be divided into:

1. Colloid (endemic)
2. Diffuse, with hyperthyroidism (toxic or exophthalmic goiter, Graves' disease)
3. Hypothyroidism (myxedema and cretinism)
4. Nodular (adenoma: a. with hyperthyroidism; b. non-toxic)

Tumors: (a) Benign
    (1) embryonal adenoma
    (2) fetal adenoma
    (3) Hürthle cell tumor
    (4) papillary cystadenoma
  (b) Malignant
    (1) metastatic papillary adenocarcinoma (lateral aberrant thyroid)
    (2) metastasizing adenoma
    (3) papillary adenocarcinoma
    (4) adenocarcinoma

Colloid goiter is the simple, common type, endemic in certain areas, apparently caused by iodine deficiency in both water and soil. A diffuse enlargement of the gland results, beginning usually at puberty. In time, the gland enlarges from the accumulation of colloid material in the acini, the epithelium of which becomes cuboidal or flattened. Colloid cysts may develop from rupture of acini. Grossly, the gland may be nodular from lack of uniformity of hyperplasia and colloid accumulation. The cut surface has a characteristic translucent gelatin-like appearance.

Microscopically, the follicles, which vary greatly in size, are lined by low cuboidal or flattened epithelium. Such a gland is in the involutional phase. On the administration of iodine the epithelium becomes taller and the colloid decreases.

Exophthalmic goiter is not necessarily associated with perceptible enlargement of the thyroid gland. Grossly, it is uniform in outline, rather meaty in consistency, and the cut surface is vascular and fails to show the excess colloid.

Microscopically, the picture varies in different portions. There are areas in which hyperplastic acinar elements predominate. These acini are lined with tall columnar epithelium which often projects as papillary protrusions into the acinar lumens that contain a minimum of colloid. Other areas show involution in which the acini are larger, are lined by cuboidal epithelium, and contain varying amounts of colloid which varies considerably in its staining properties. It may be vacuolated and show a typical serrated margin. A varying amount of lymphatic tissue is scattered through the gland, even including secondary follicles. The connective tissue stroma is generally irregular in distribution with thick and thin traceculae.

After the administration of iodine, the histologic picture changes. There is a general increase in colloid, which takes a more uniform stain, and a decrease in the height of the columnar epithelium of the acini. Thiouracil, on the other hand, produces a different histologic picture. There is a decrease in the amount of colloid and the epithelium becomes even more generally hyperplastic in character. In non-toxic types of adenomas the picture in the hyperplastic areas is more that of adult gland tissue without the basal individual cells and papillary formation.

The **benign neoplastic adenomas** might be mentioned here since these nodules are similar clinically to the nodular goiters on direct examination and present a history that indicates no thyroid hyperactivity. In EMBRYONAL ADENOMA the embryonal cells are arranged in solid cords and groups with little or no acinar formation, and the mass is surrounded by a well defined capsule. The second is the FETAL ADENOMA in which the well encapsulated nodule shows small acini made up of cuboidal and low columnar cells. There is little or no colloid and some of the cell groupings without lumens resemble rosettes. The HÜRTHLE CELL TUMOR produces similar nodular enlargement. Microscopically, the tumor cells are large with eosinophilic cytoplasm and show some abortive attempt at acinar formation. There may even be small masses of colloid. The cells resemble somewhat those of the liver and the cortical cells of the adrenal. Their origin is not clear but it is highly probable that they represent stages in the evolution of the neoplastic thyroid cell. Cells of this type are also seen in Hashimoto's struma.

Metastasizing papillary cystadenoma is of considerable interest and importance. It is not uncommon to find in the lymph nodes of the neck, lateral to the thyroid, foci of thyroid tissue with a papillary and cystic arrangement. These have been considered aberrant particles of thyroid tissue, but in every instance which has been thoroughly studied a similar tumor has been demonstrated in the parent gland. Therefore, when such a lateral aberrant mass is discovered, the thyroid is carefully examined for an adenomatous focus and the involved lobe is removed. If these lateral foci are considered metastases, then the tumor must be considered malignant, although the incidence of further metastasis is very low. This lesion has been seen in children, and recently a series was reported by Winship.

Microscopically, aside from a usually well developed fibrous capsule which constitutes the wall of the cyst, there are papillary elements covered by a single layer of cuboidal epithelium. The cells show more pleomorphism than the papillary elements in toxic goiter and they are generally lower. The papillary nature of the malignant adenoma is much more complex than that of the toxic or simple adenoma.

There are two schools of treatment for this lateral lymph node involvement; one advocates radical neck dissection, the other prefers to limit operation to removal of the lymph node and the involved lobe of the parent gland.

Frank **carcinoma of the thyroid** represents a confusing picture and begins with the so-called blood vessel-invading adenoma in which the epithelial elements are well defined. It is only by the presence of gland elements within the vessel lumens that such a carcinoma can be differentiated from a benign tumor. Others are more frankly malignant histologically and usually present papillary features, but the cytologic character may vary from the squamous type to an undifferentiated small cell type which is difficult to distinguish from sarcoma. There is a special giant cell carcinoma which seems to be particularly malignant clinically and which also may be mistaken for sarcoma. It is a tumor of advanced years and grows rapidly. In addition to the enormous cells, usually with a single nucleus, there are spindle cells that suggest fibrosarcoma.

Because of the rich blood supply of the thyroid gland, the prognosis of carcinoma is particularly unfavorable; it can metastasize through both lymphatic and blood channels. By the latter route, the favorite sites of metastasis are the lungs and bones.

One of the most difficult tasks which confronts the pathologist is to determine by histologic examination whether a given thyroid is, first, the seat of malignant tumor, and second, what the probabilities are of metastasis.

PARATHYROID GLANDS

There are usually four parathyroid glands, two located on the medial part of the dorsal surface of each lobe of the thyroid, the other two near the lower poles of the lateral lobes. Additional nests of parathyroid tissue may be embedded in the thyroid or scattered along the capsule. Occasionally they may be found in the thymus.

Hyperplasia, or, better, **hyperactivity of the parathyroid tissue,** leads to disturbance of calcium and phosphorus metabolism. The former is elevated and the phosphorus is reduced in the blood serum. Clinically it is manifested in some instances by the syndrome of OSTEITIS FIBROSA CYSTICA (VON RECKLINGHAUSEN'S DISEASE OF BONE), and in others by CALCINOSIS OF THE RENAL PARENCHYMA and the formation of renal calculi. This may or may not be accompanied by bone changes. The serum alkaline phosphatase is elevated in the von Recklinghausen syndrome. This hyperactivity is practically always due to an adenoma. The tumor may involve a gland in its normal location, or, as Castleman and Mallory have reported, it can be ectopic, especially in the upper mediastinum.

Microscopically, the tumor may consist predominantly of the darker, smaller chief cell or the larger vacuolated cell, or it may show a mixture of the two. Some are made up of acinar elements of cuboidal cells and resemble the fetal adenoma of the thyroid.

Hyperplasia may be secondary to a chronic kidney disease, especially of children. The hyperplasia results in bone changes that have been called RENAL RICKETS. They are similar to the changes in von Recklinghausen's disease. When it occurs in young individuals with "growing" bones, deformities result.

Decrease of parathyroid hormones again disturbs the phosphorus and calcium metabolism, increasing the former and decreasing the latter in the blood serum. This results in the clinical syndrome of TETANY.

CARCINOMA is rare, but several instances of metastasizing tumors have been reported.

CAROTID BODIES

The carotid bodies are situated in the bifurcation of the common carotid arteries. Their function is not understood, but they have histologic characteristics of the glomus, of the adrenal, and of Zuckerkandl's organ, all concerned in the sympathico-chromaffin complex. The peculiar vascularity and the chromaffin character of some of the cells indicate this relationship.

The **carotid body tumor** occurs in adult life. It is deeply situated, and its association with the bifurcation of the common carotid artery permits lateral movement but restricts up and down motion. It is benign, of very slow growth, and is not accompanied by endocrine manifestations. It grows upward in the neck and may come to impinge on the base of the skull. Histologically, it mimics the features of the carotid body, being composed of prominent vascular spaces which are bordered wholly or in part by large epithelioid cells that have an acidophilic and sometimes vacuolated cytoplasm. Their chromaffinity is not always demonstrable. Some pathologists class the tumor with the pheochromocytoma of the adrenal; others, with cutaneous glomus tumors and paragangliomas.

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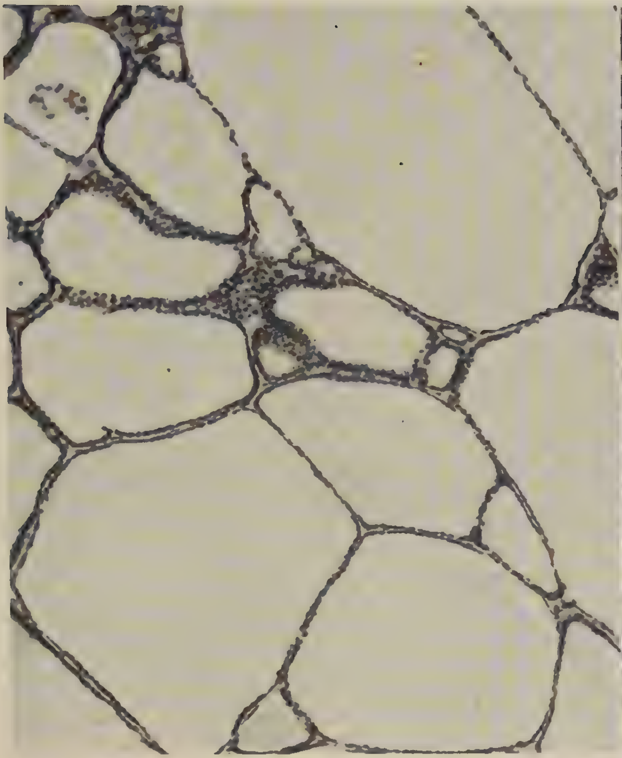
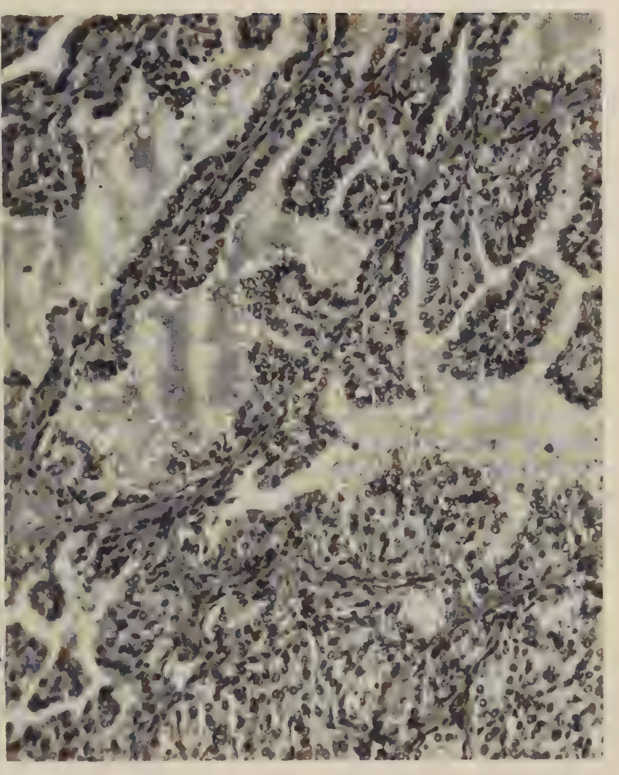
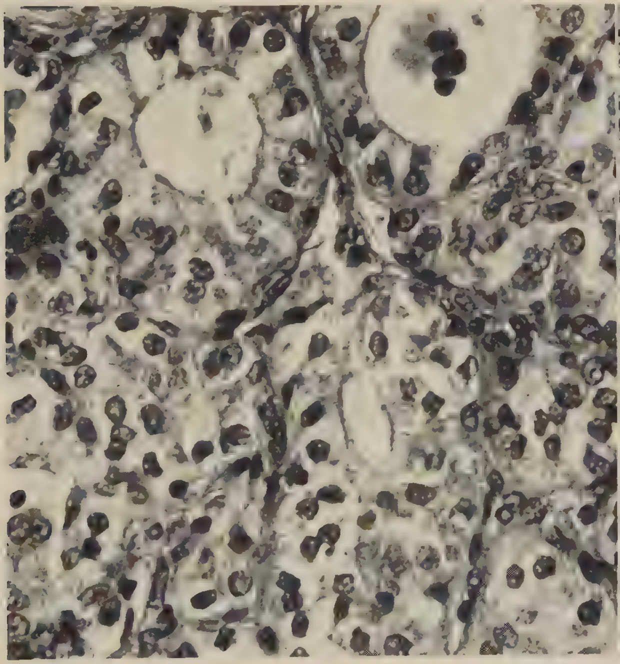


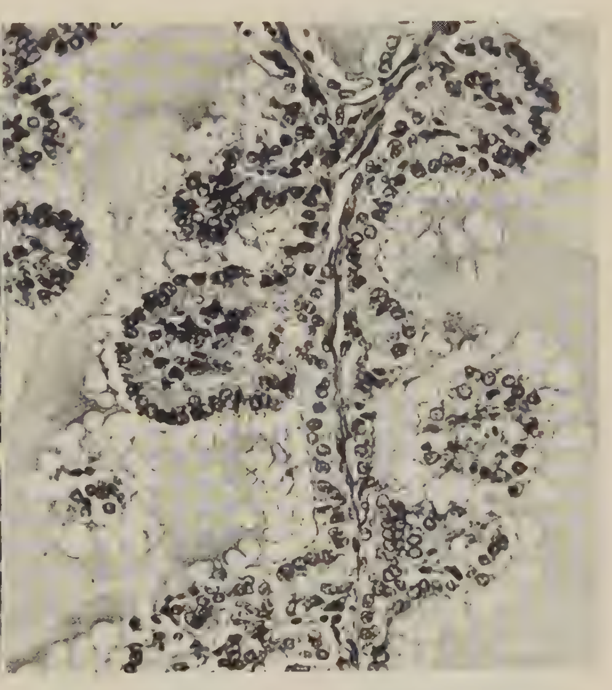
Relatively normal so-called **involution.** Acini lined by low cuboidal cells; colloid not in excess and neuriform in character. x 125.



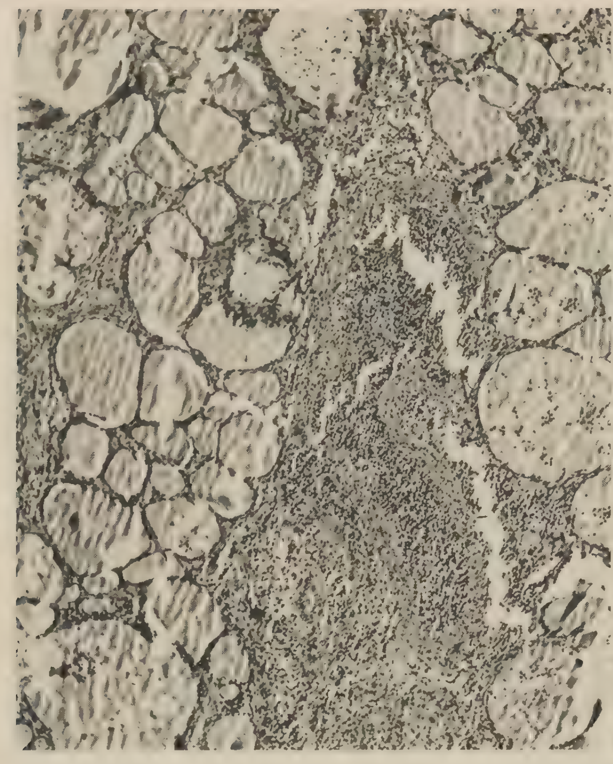
Hyperplasia, toxic goiter. Solid and papillary forms, as they occur in adenomas. x 145.



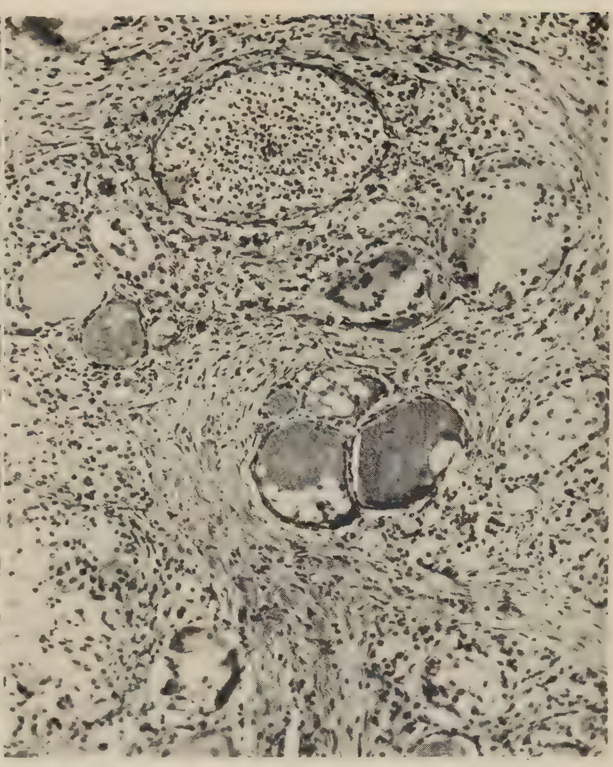
Hyperplasia, solid form, may be of trabecular type (lower portion) or colloid-free acinar type. x 400.



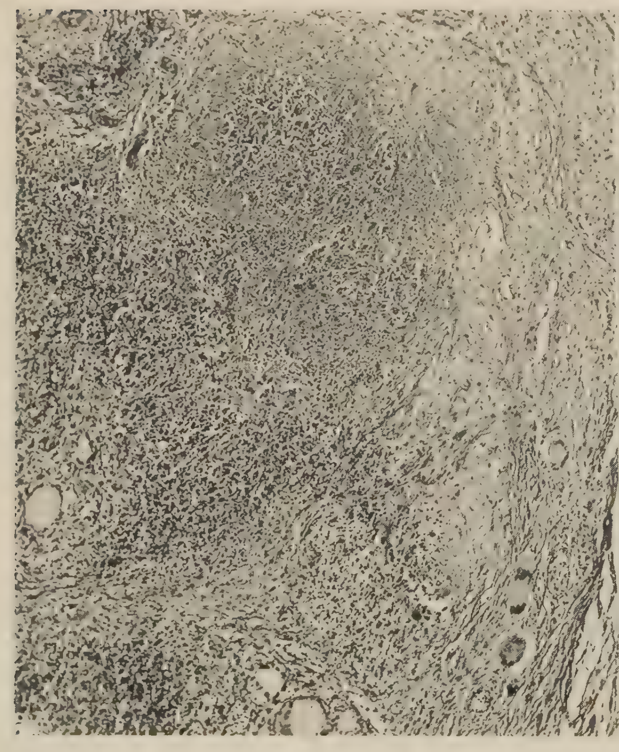
Papillary hyperplasia must be distinguished from malignant papillary carcinoma. In hyperplasia the papillae are simpler in structure and the epithelium is uniform. The vacuoles are in the colloid, not in the cells. x 275.



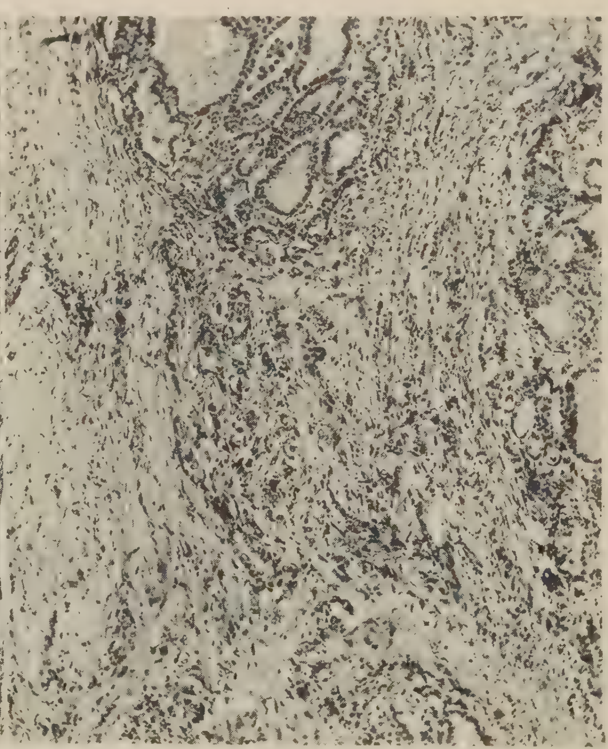
Suppurative thyroiditis. Focus of heavy exudate among normal acini. Abscess may develop. x 70.



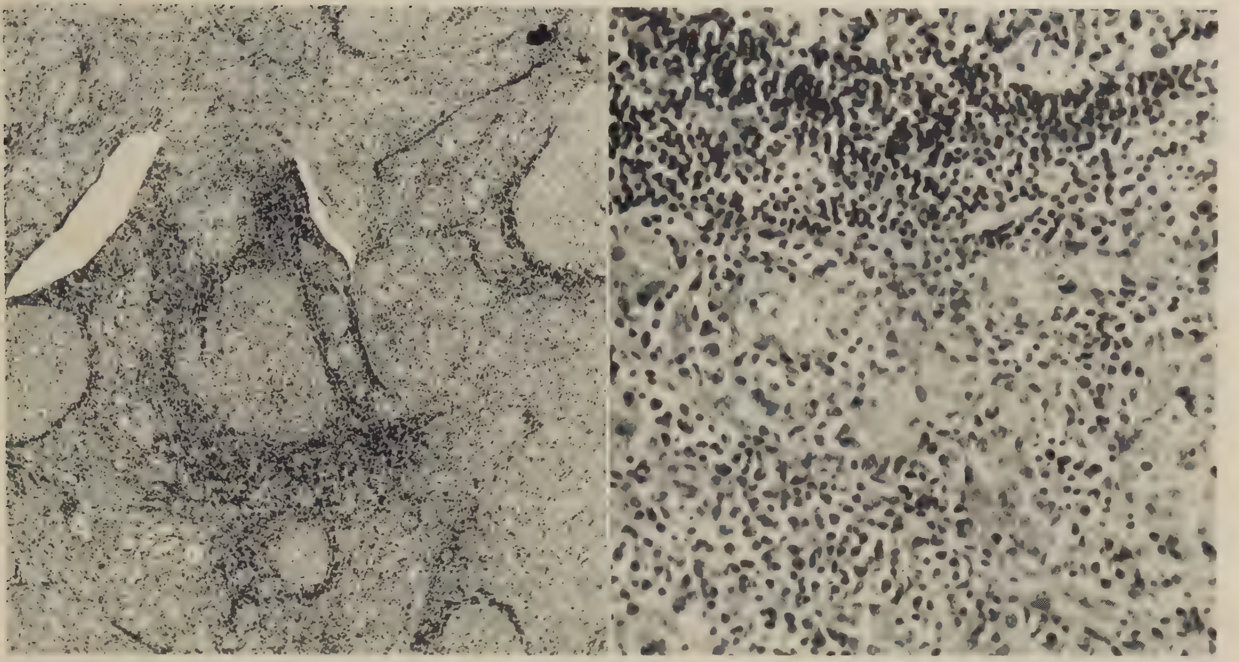
Subacute thyroiditis. Fibrosis with destruction of acini. The liberated colloid stimulates foreign-body tubercle formation (lower left). x 125.



Tuberculosis. Involvement of thyroid in a general miliary infection. There are several miliary tubercles, one showing caseation. x 70.



Inflammation in a hyperplastic thyroid. Fibrosis has isolated and compressed the acini, simulating infiltrating carcinoma. x 240.

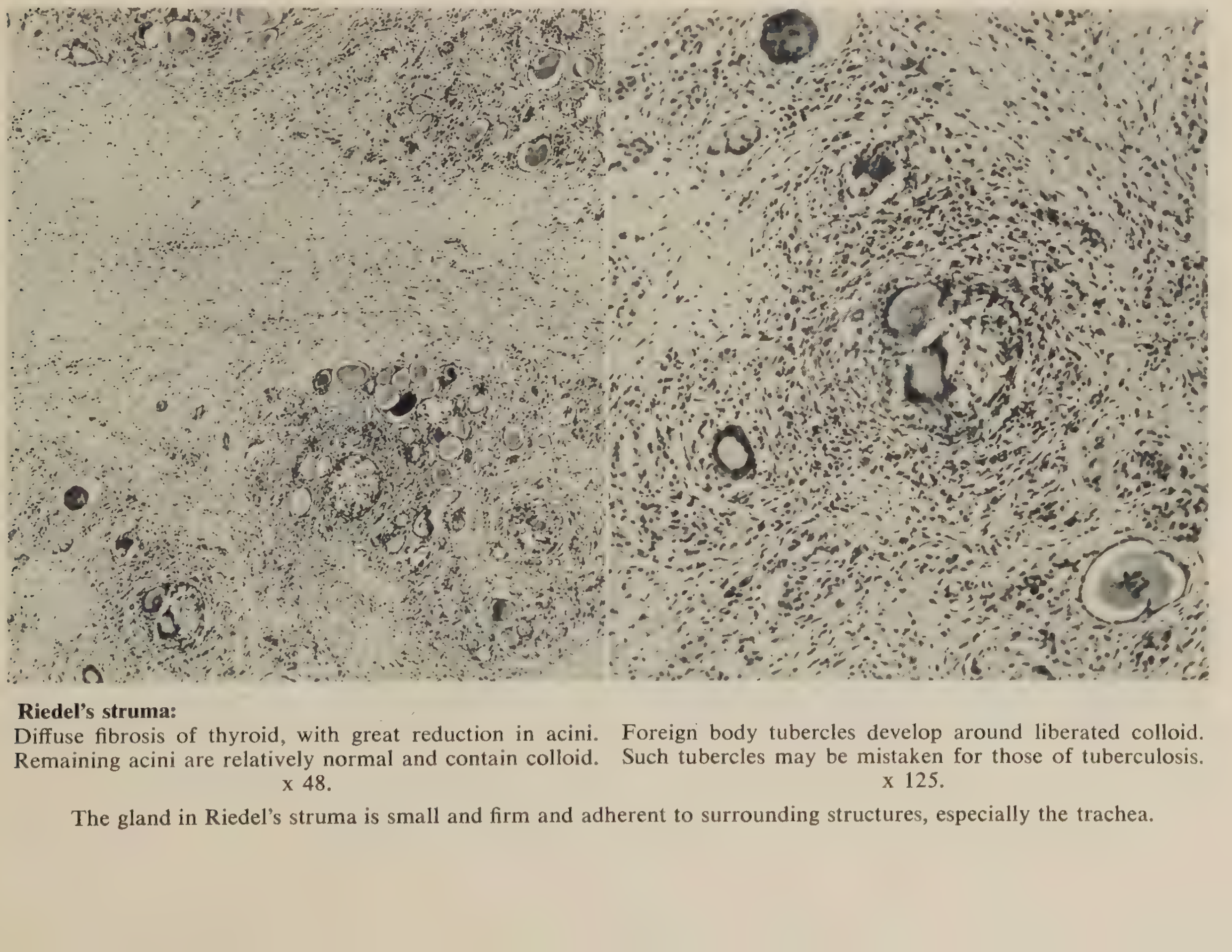


Hashimoto's struma:

Uniform infiltration by lymphocytes, with varying amounts of plasma cells. Numerous secondary lymphatic follicles and increase in fibrous trabeculae, producing distinct lobulation of the gland. x 48.

Great reduction of acini; virtual absence of colloid. The remaining gland cells are of the Hürthle type. x 275.

The gland in Hashimoto's thyroiditis (struma lymphomatosa) is enlarged and is not attached to surrounding structures.

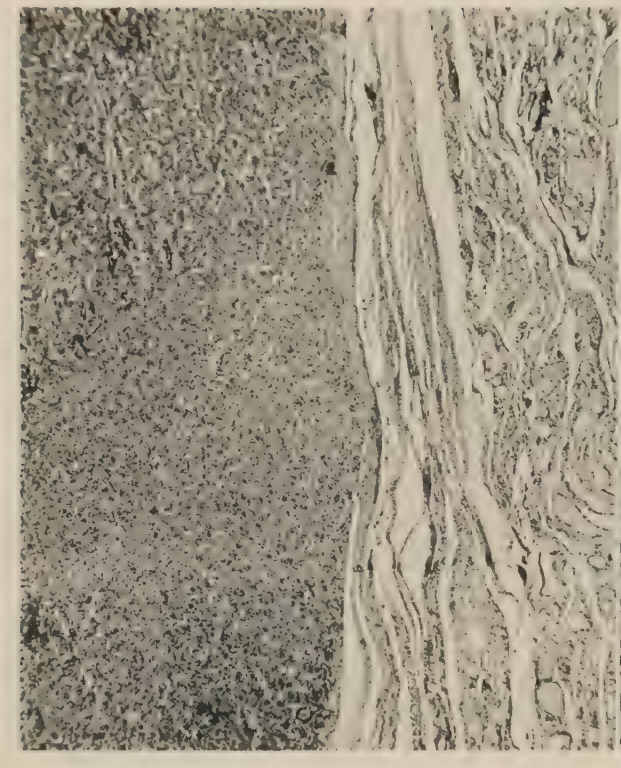


Riedel's struma:

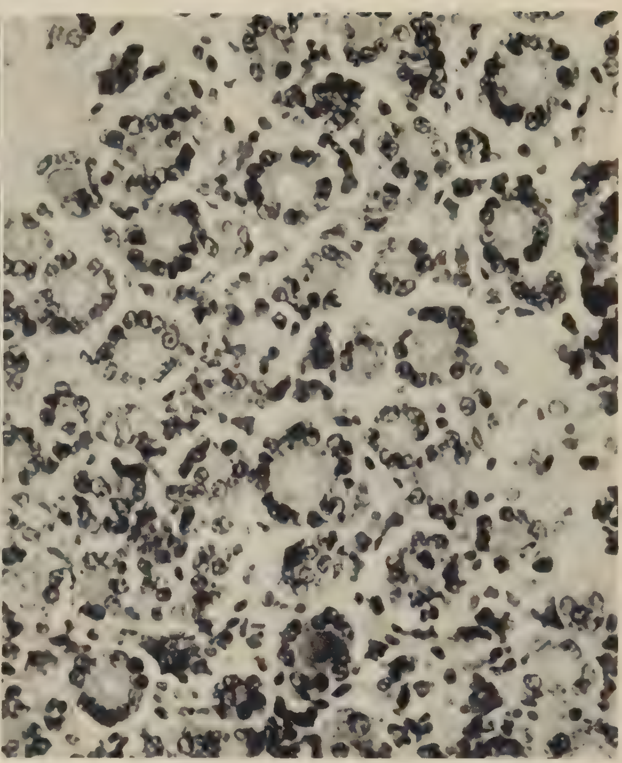
Diffuse fibrosis of thyroid, with great reduction in acini. Remaining acini are relatively normal and contain colloid. x 48.

Foreign body tubercles develop around liberated colloid. Such tubercles may be mistaken for those of tuberculosis. x 125.

The gland in Riedel's struma is small and firm and adherent to surrounding structures, especially the trachea.

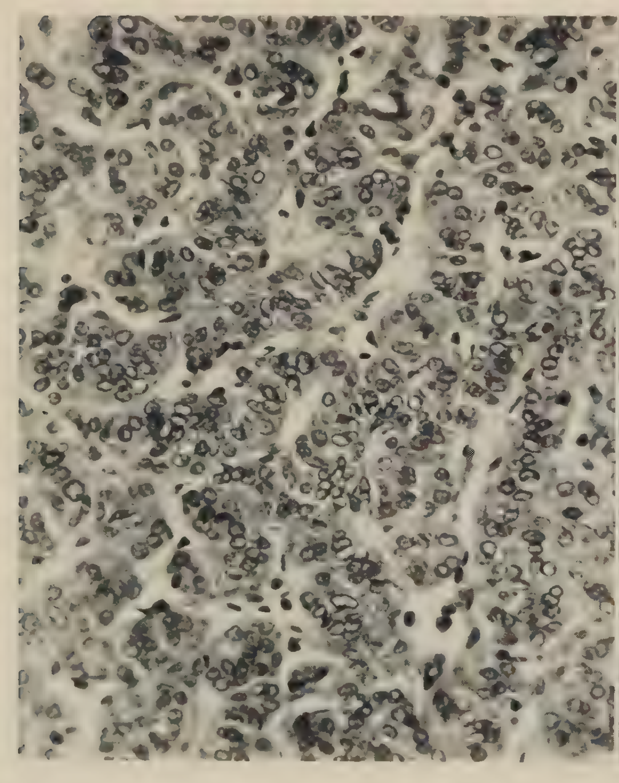


Embryonal adenoma. Cells of cuboidal type, but little evidence of acinar arrangement and no colloid. x 48.

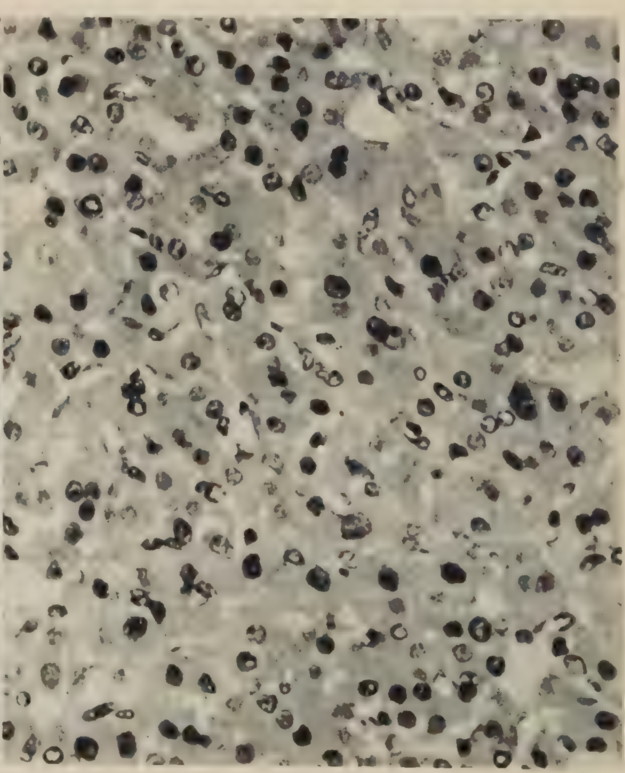


Fetal adenoma; small acini, little or no colloid. x 400.

Adenomas of thyroid are generally well encapsulated masses in one lobe and are benign.



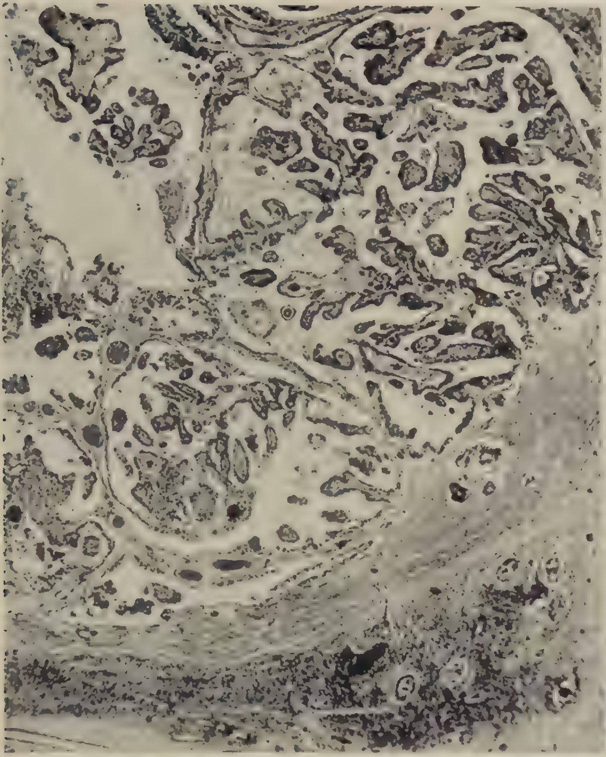
The cells in embryonal adenoma may have a solid trabecular arrangement. x 275.



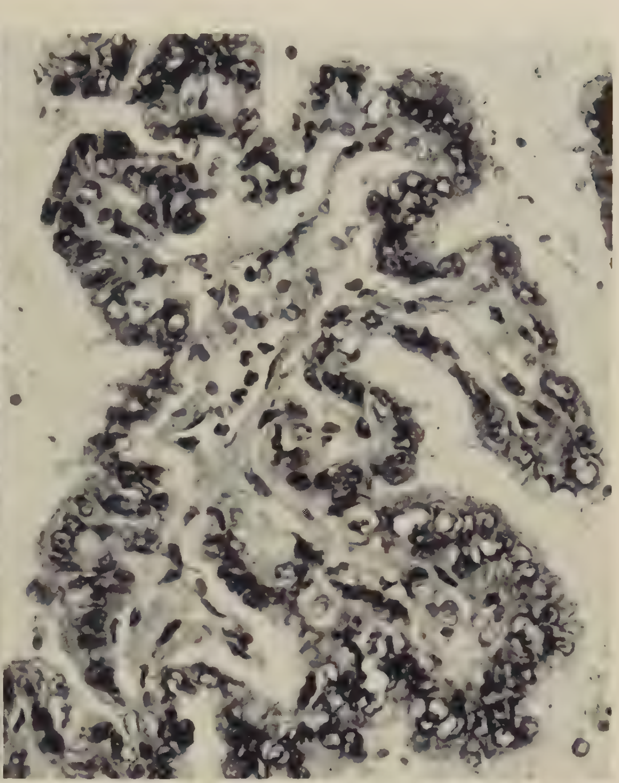
Hürthle cells, usually in acinar arrangement without colloid, have relatively large amounts of pale cytoplasm. x 400.

PAPILLARY CARCINOMA, THYROID

(LATERAL ABERRANT THYROID)

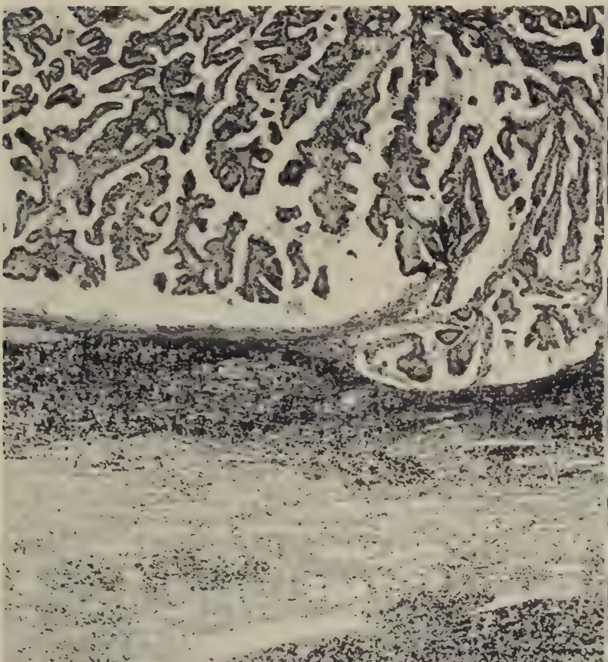


Papillary carcinoma, thyroid gland, similar to a tumor of a cervical lymph node on the same side. x 48.

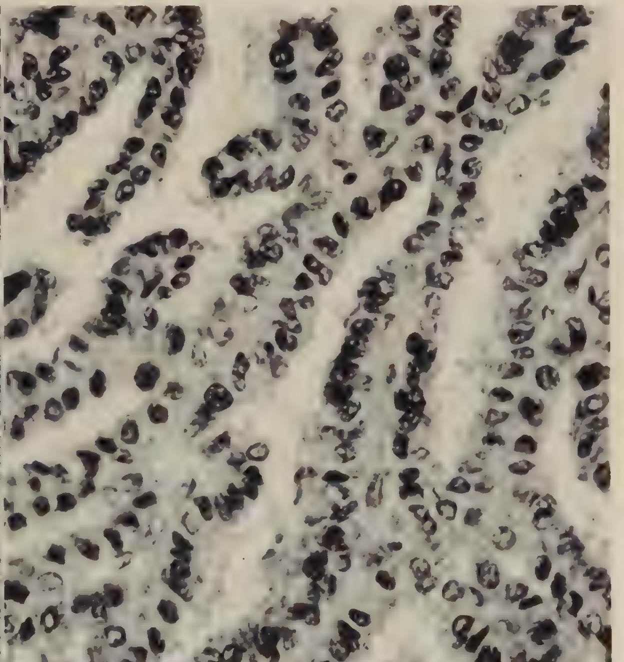


Multilayered neoplastic epithelium of the papillary carcinoma. x 400.

Not all papillomas of the thyroid are malignant. Benign ones develop in the hyperplastic toxic gland.

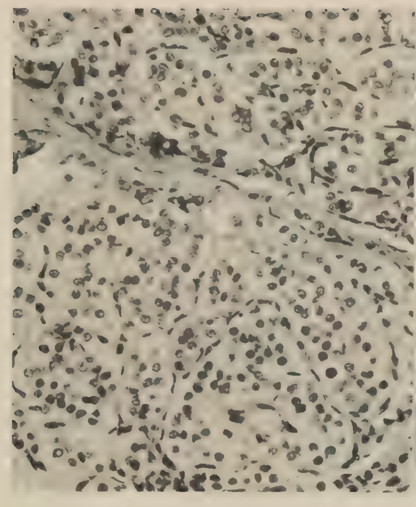


Papillary carcinoma, so-called lateral aberrant thyroid, obviously in a lymph node. x 48.

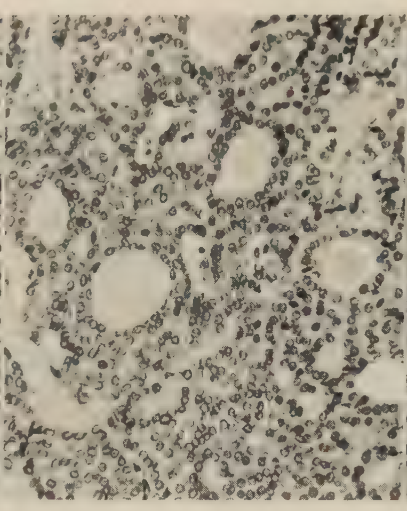


The cells are not as "wild" as in the case above, but they are multilayered and of neoplastic type. x 400.

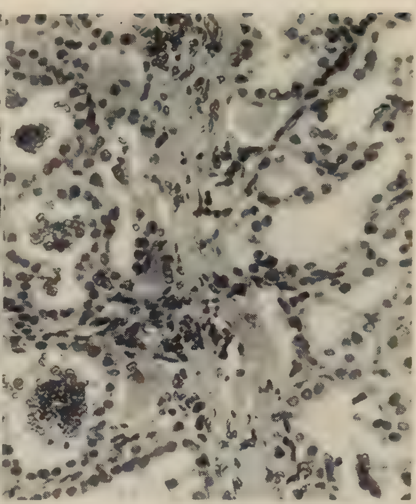
These carcinomas at times result in widespread metastasis.



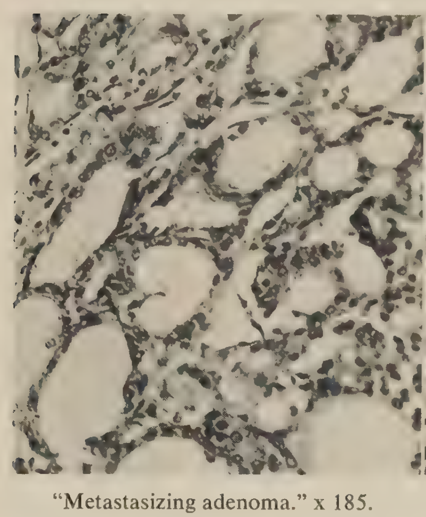
Solid trabeculated type. x 165.



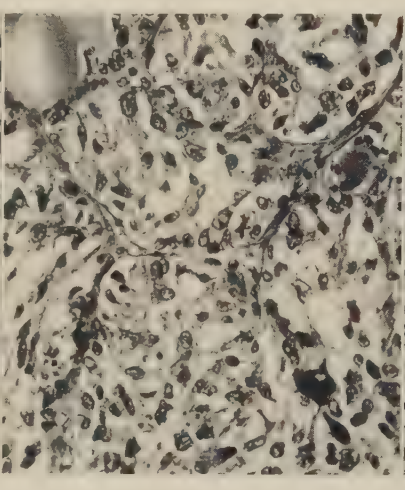
Follicular adenocarcinoma, metastasized to bone. x 180.



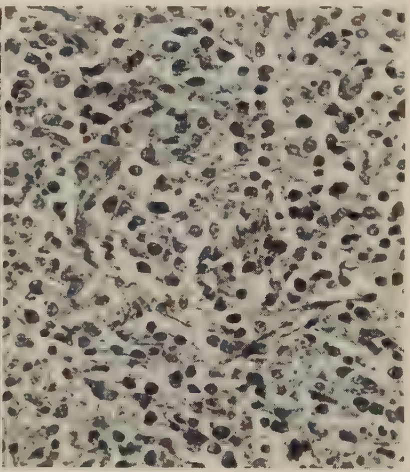
Adenocarcinoma in a lymph node. x 290.



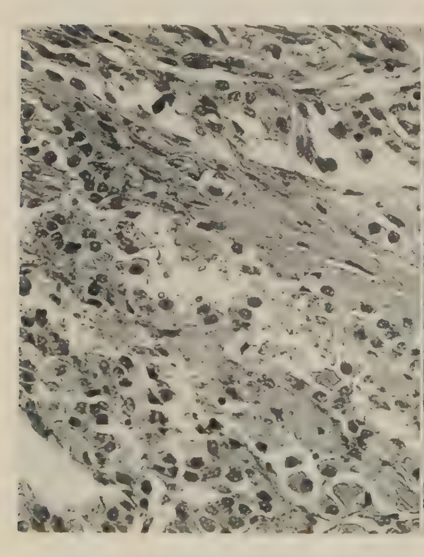
"Metastasizing adenoma." x 185.



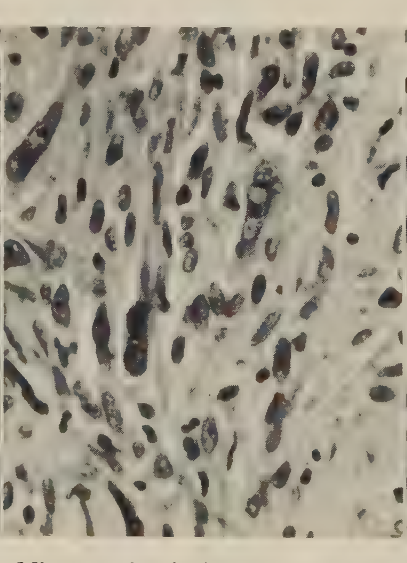
Carcinoma of alveolar type. x 200.



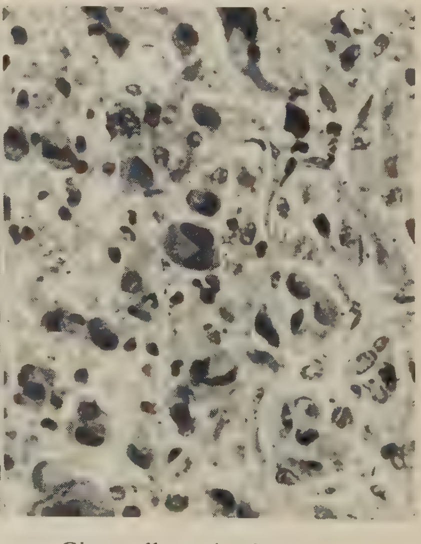
Small cell type with no special arrangement. x 285.



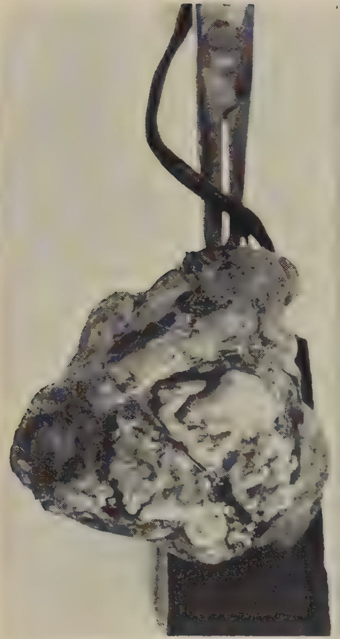
Mixture of Hürthle and spindle cells. x 250.



Mixture of spindle and giant cells. x 350.



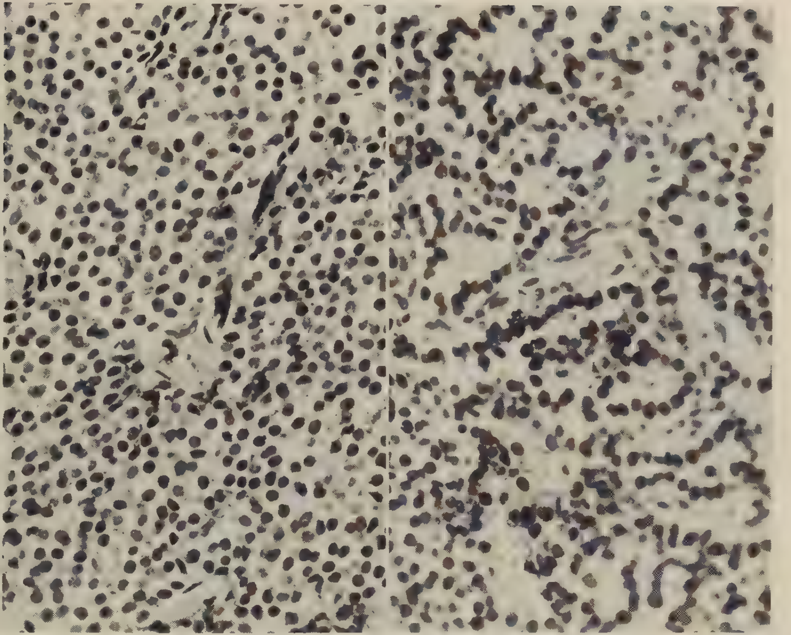
Giant cells predominate. x 515.



Parathyroid adenoma, largely necrotic, removed from 48 year old woman.

Symptoms of several months' duration suggested hypoparathyroidism.

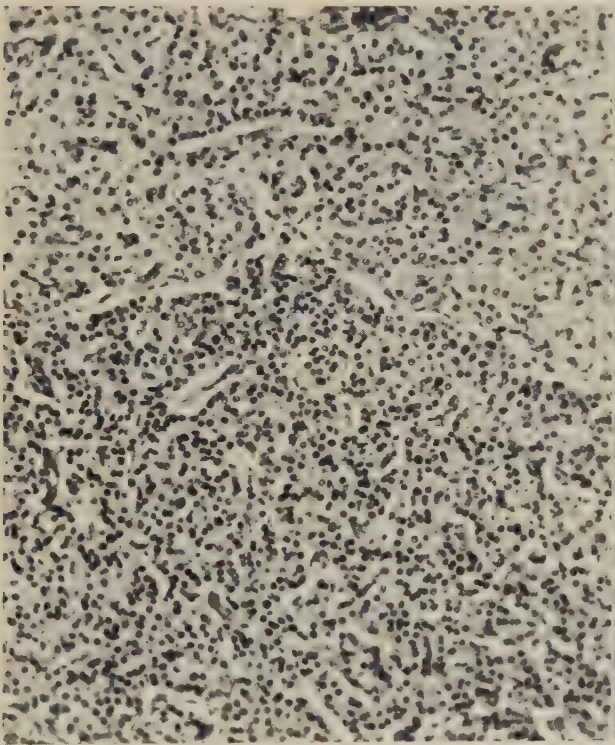
Blood calcium—5.0 mg. per 100 cc., dizziness and convulsions.



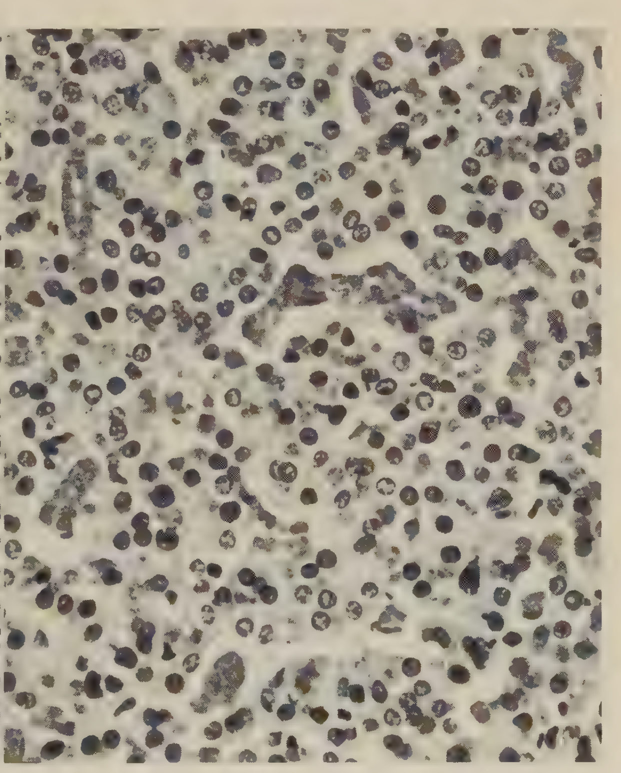
Parathyroid adenoma, from a 59 year old man with osteitis fibrosa cystica of long duration. Blood calcium 20 mg. and phosphorous 1.7 mg. per 100 cc.; renal calculi were present. The adenoma was removed, but recurred.

Cells in this portion of another adenoma are indistinguishable from those of the normal gland. x 285.

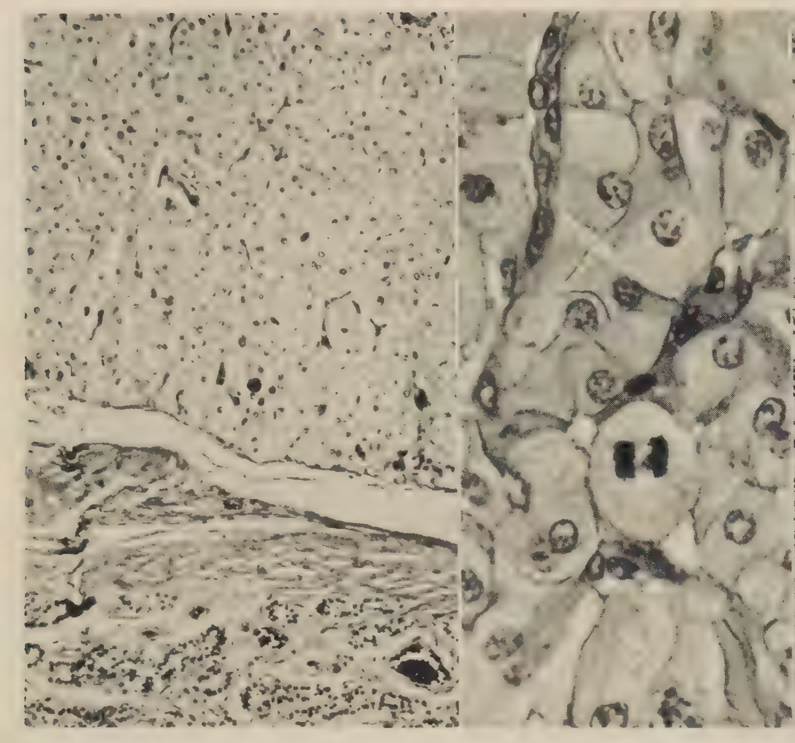
Cells in other areas are definitely neoplastic and tend toward acinar arrangement. x 285.



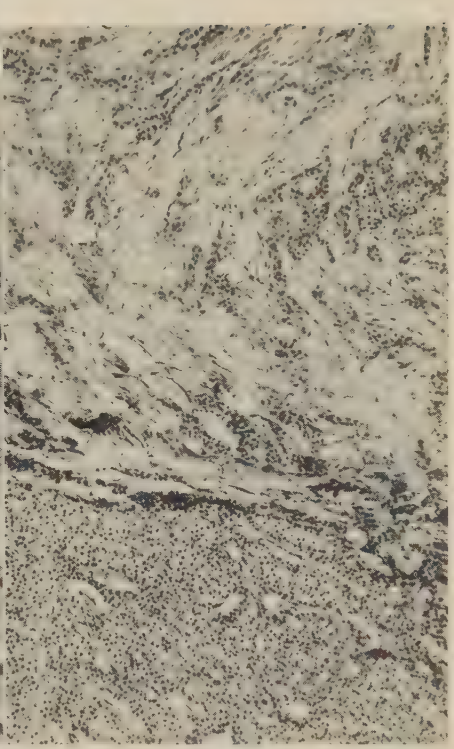
Adenoma with hormonal activity:
Area containing neoplastic cells above tissue that appears normal. x 125.



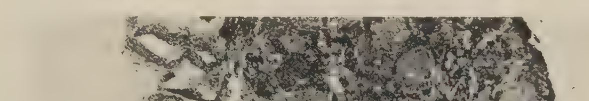
Large acidophilic cells with irregular and hyperchromatic nuclei. x 400.



Adenoma, from a 23 year old woman without clinical symptoms; normal blood calcium and no bone changes. The tumor was embedded in the thyroid and originally was diagnosed Hürthle cell adenoma. The adenoma compressed the parathyroid, seen below the capsule. x 85. Enormous acidophilic cells, hormonally inactive. Mitotic figure in center. x 700.



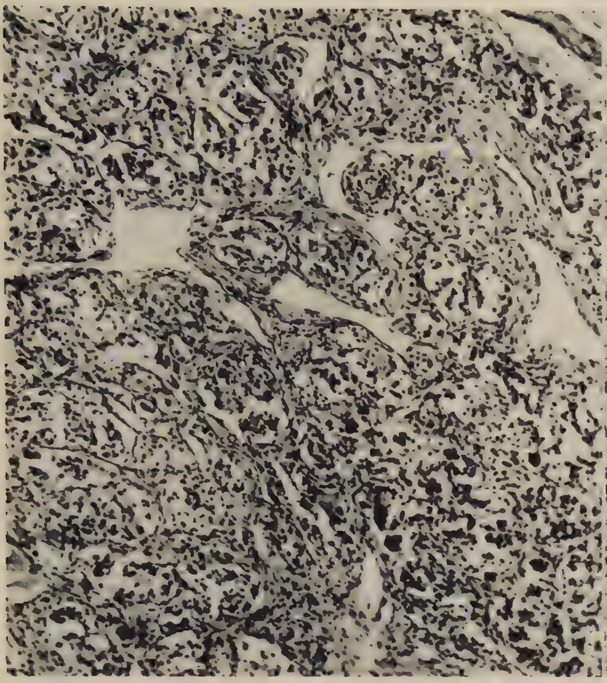
Malignant adenoma, small type cell, that also involved the thyroid. More normal parathyroid at bottom. x 85.



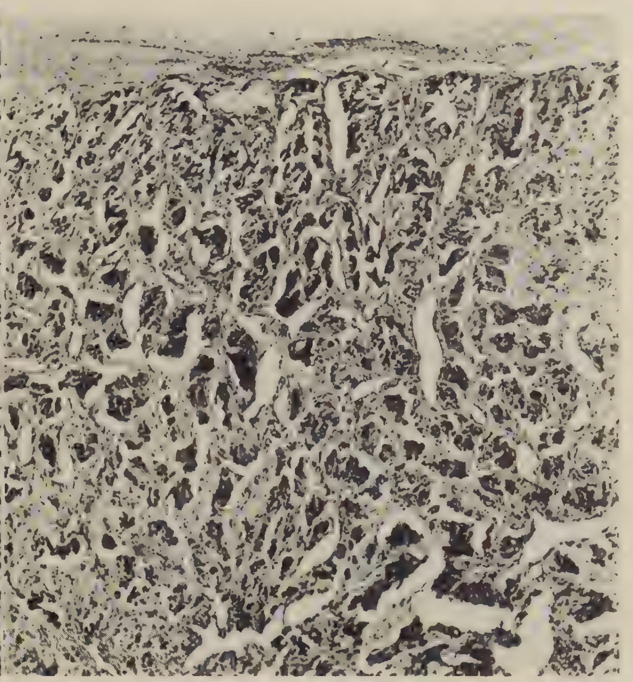
Parathyroid cysts, from an elderly man:
The cystic process in this gland appears to be a pseudocyst (degeneration). x 13.

Retention cyst, in the other gland, is filled with colloid of unidentifiable structure. x 16.

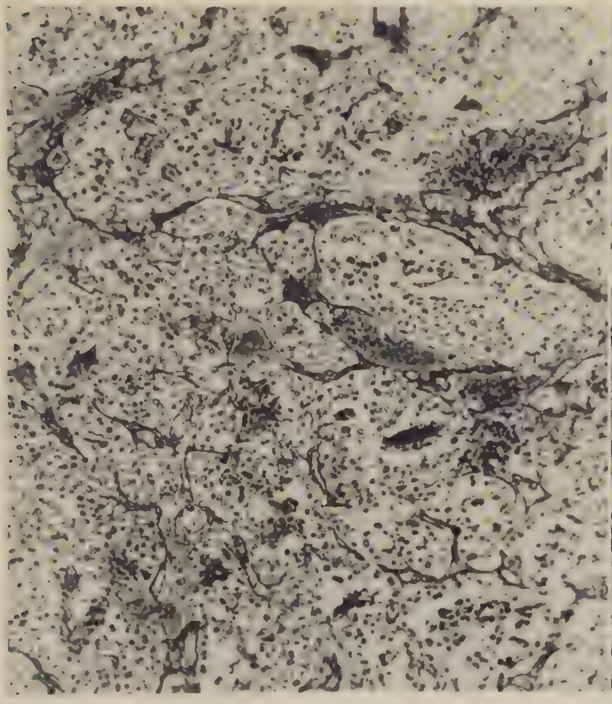
Cysts of parathyroid are usually small and do not produce symptoms. They occur in adenomas as a result of degenerative changes.



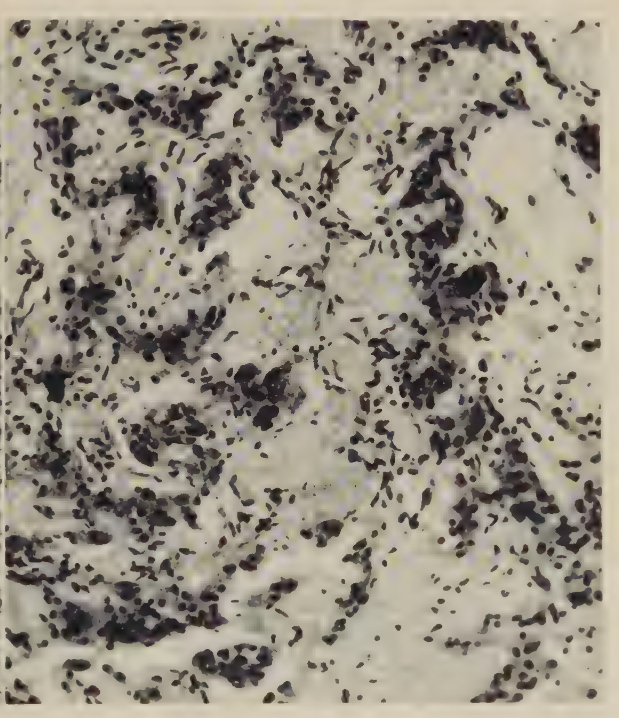
Characteristic pattern of **carotid body tumor.** Groupings of fairly uniform, clearly defined cells, in close association with a prominent vascular network. x75. Soft oval tumor, 2 x 3 cm., from right side of neck of a 54 year old woman. x18.



Well encapsulated tumor from site of right **carotid body** of a 51 year old woman. Nests of cells with hyperchromatic nuclei, which vary in size and shape, and a more prominent characteristic vascular pattern. x55. At time of operation the tumor had been present one year; systolic blood pressure was 180 and dropped to 120 postoperatively. (South Bend Medical Foundation, Inc., Ind.) x18.



Typical cellular grouping of carotid body tumors, clearly demonstrated with reticulum stains. x125. Oval tumor, 3 x 3 cm., discovered accidentally deep in right side of neck of a 50 year old woman. (Lexington Clinic, Ky.) x18.



Tumor showing considerable variation in nuclear size and shape. x185. An aggresive tumor which extended to cranial cavity, causing compression of third ventricle and fatal hydrocephalus. No metastasis. (F. Foucar, Washington, D.C.) x18.

CHAPTER 30

SALIVARY GLANDS

Included among the salivary glands are not only the parotid, submaxillary and sublingual glands, but a large number of small collections of mucoserous glands scattered through the mucosa of the lips, palate and cheeks. This distribution is important in a consideration of the mixed tumors of the salivary gland type and retention cysts. Inflammatory reactions, however, are uncommon in the small scattered gland groups.

Stenosis of the main duct of the major salivary glands is a common precursor of inflammation—**sialadenitis.** Such inflammations are usually low grade bacterial infections that may, through chronicity, lead to extensive fibrosis of the glands and atrophy of much of the parenchyma. Histologically, and in addition to these features, there is a heavy infiltrate of small mononuclear cells with a sparse content of polymorphononuclear leukocytes.

It is necessary in appraising the clinical enlargement of a major salivary gland to distinguish between chronic inflammation and enlargement from occlusion of the duct. Generally with duct obstruction there is a cyclic enlargement, an important diagnostic feature. The parotid gland is frequently involved by chronic inflammation because the orifice of Stenson's duct is more exposed and larger than the openings to other major glands, but serious chronic inflammations are commonest in the submaxillary glands.

Specific granulomatous infections include TUBERCULOSIS, which is most common in the parotid. The infection is usually a direct one from contaminated sputum. ACTINOMYCOSIS occasionally involves the parotid gland as a primary site.

MIKULICZ' DISEASE is a classic syndrome which has lost some of its specificity through the years. As originally described, it was considered to be a tumor-like accumulation of lymphatic tissue in any of the several salivary glands and also in the lacrimal glands, which are histologically and physiologically modified salivary glands, although entirely serous in type. The syndrome is characterized clinically by the simultaneous and painless enlargement of several glands in the group. The acini are widely separated by the infiltrate and become atrophic, in time, from pressure. There is usually an increase in connective-tissue stroma which tends to divide the glands into lobules. It is definitely established now that Mikulicz' disease is not neoplastic but inflammatory, and the present tendency is to include any condition which produces a simultaneous enlargement of several of the salivary glands in the syndrome. These may include granulomatous inflammations or a neoplasm, such as lymphosarcoma.

Another syndrome in which the parotid glands are involved is UVEO-PAROTITIS. In this, Heerfordt's syndrome, a febrile condition with bilateral iridocyclitis and bilateral parotitis comprises the clinical picture. Pathologically, uveo-parotid fever is one of the localized manifestations of sarcoidosis (see Chapter 2).

The important acute inflammatory condition in the salivary glands is MUMPS, a viral disease which, in most cases, affects the parotid glands of one or both sides. Pathologically, the gland is densely infiltrated with cellular exudate, edema, congestion, and hemorrhages. The epithelium of the ducts and acini is swollen and vacuolated and some of the gland structures undergo necrosis. Inclusion bodies can usually be seen in the affected epithelium. In the later stages there is less of the exudative element but more of the degenerative change and hyalin accumulation.

It must be remembered that mumps is not a local disease of the salivary glands. The virus has a tropism for other glandular structures, especially the pancreas, itself a modified salivary gland, and the gonads, more commonly the testes than the ovaries. As in other viral diseases, such as measles and chickenpox, encephalitis is occasionally a complication. Haymaker and Smadel have described several such complications of the simple viral diseases, including mumps. Deafness may also be a complication, in fact, mumps is said to be the foremost cause of unilateral total deafness.

The salivary glands, again most commonly the parotids, are not infrequently the seat of specific and secondary inflammations in infectious diseases, particularly typhoid fever and typhus fever.

Calculi (sialoliths) sometimes develop in the ducts or body of the salivary glands, especially the submaxillary glands. The stones may have nuclei of foreign bodies, or bacterial or fungal growths. The calculi are readily demonstrated by x-ray.

Simple **retention cysts** are very common in the lips and cheeks and on the under surface of the tongue. They are usually small, but excision seems to be the only certain method of eliminating them. Histologically, they are lined by flattened cuboidal or squamous epithelium and they usually contain cholesterol.

A more definite clinical entity, RANULA, has been associated with the sublingual gland. This is a cyst that develops in the floor of the mouth under the tongue. Its wall is so thin that it gives to the overlying mucosa the "frog belly" appearance and color —a diagnostic feature. The simplest explanation is that it is the result of obstruction of the main duct of the sublingual salivary gland. However, evidence seems to indicate that it is more likely the dilated remains of the cervical sinus, and in some instances the cyst can be traced up to the base of the skull. On the other hand, if it were a salivary gland duct, the secondary ducts of the gland would be dilated, which is not the case.

TUMORS OF THE SALIVARY GLANDS

The commonest tumor of the salivary gland is the so-called **mixed tumor,** usually seen in the parotid. However, it is also found in the submaxillary and sublingual and in the mouth, particularly in the palate and lip, and in the skin. Ash, in a review of 798 mixed tumors of the salivary-gland type, reported that 503 were in the parotid gland, 55 in the submaxillary, and only two in the sublingual. Twenty-nine were central tumors of the maxilla or mandible. It is a tumor about which much controversy has raged through the years. It is called mixed tumor because it contains both epithelial elements and mesenchymal or connective tissue elements. The great argument has been over the histogenesis of this peculiar combination of tissues. It is generally conceded now, however, that these elements are all of epithelial origin and that the glandular epithelium peculiar to the salivary glands and to some of the other glands of the body, those of skin and breast particularly, are capable of producing an intercellular substance of the nature of chondromucin, which can go on to differentiation to cartilage and bone.

The variety of the cell picture is legion. The epithelial element ranges from the well differentiated and orderly glandular type to the primitive, undifferentiated basaloid type. There may even be areas of squamous cell differentiation. The mesenchymal element may vary from thin mucin to well developed bone. This multiform cytologic picture has led through the years to a complex nomenclature.

The tumor commonly comes to attention in middle life as a slowly enlarging mass which is generally well encapsulated, especially if it is in an advanced stage or is a recurrence following surgical removal. It is comparatively benign, despite the highly cellular, widely growing appearance which it shows at times histologically. If the entire capsule can be removed the prognosis is favorable, but metastasis does occasionally occur, perhaps many years after the discovery of the primary tumor. It has been the experience in the Registry that the mixed tumors of the palate have a much more unfavorable prognosis than those of the salivary glands. In this situation, the tumors tend to invade, are not encapsulated to the extent that the salivary-gland tumors are, and therefore they are difficult to remove completely. They will recur and may destroy the bony structures and invade the nasal cavity and the maxillary sinuses. There are several instances in the Registry of metastasis to the cervical lymph nodes and lungs. The variations in the histologic picture are shown in the illustrations that follow.

Although it is not generally recognized that a close histogenetic, pathologic and clinical relationship exists between the mixed tumor of salivary glands and the adenoma of bronchial type, our study of the many cases of these lesions in the Registries has given us such an impression. Examples from the sinuses, pharynx, larynx, trachea and bronchi are shown in the illustrations.

Recently Stewart and his colleagues were able to separate from the group of salivary-gland tumors a separate entity which has been termed **muco-epidermoid tumor.** This tumor is entirely epithelial and seems to develop from the duct epithelium. It may be either solid or cystic, encapsulated or not. Histologically, it is made up of masses of cells which contain both columnar elements that will produce mucin and cellular elements that tend to differentiate toward the squamous. This group, so far, has shown less tendency to manifest malignant features than the mixed tumor, although frank carcinoma has been reported as developing in some.

Adenocarcinoma of the salivary glands can be separated from the tumors already discussed. These tumors usually grow rapidly and metastasize early. They are entirely epithelial and do not include the mesenchymal features of the mixed tumor. The cells may retain an adenomatous character or they may be present in islands and strands of undifferentiated cells, usually of a spindle type. This last feature can be so marked as to simulate fibrosarcoma.

Papillary Cystadenoma Lymphomatosum. — Another tumor that is very specific, histologically and clinically, is generally associated with the salivary glands, particularly the parotid. It is frequently called Warthin's tumor in American literature, although it was recognized years before Warthin's publication in 1920. It is a tumor of later life and occurs predominantly in males. Although usually embedded in a salivary gland, it has been seen in adjacent soft tissues of the neck. In one Registry case the tumor was found at operation deep in the right side, anterior to the sternocleidomastoid muscle and several centimeters below the ear. In a second case, the tumor was below the right parotid gland. On the other hand, in the examination of a great many salivary glands, microscopic masses of lymphoglandular tissue identical with Warthin's tumor have been found, and one of these is included in the illustrations.

The tumor is slow-growing but may reach a considerable size. It is generally benign, but there have been at least two reports of malignant change.

Warthin attributed its origin to the eustachian-tube anlage. Others consider it to arise in a branchial cleft, while still others favor the salivary glands. As the result of the study of several cases in the Registry, it seems most likely that they are of branchial-cleft origin and that their relation with the parotid gland is accidental. The gland element resembles very closely the adenomas that arise in the ceruminal glands of the external auditory canal, but they differ from these tumors by the invariable presence of abundant lymphatic tissue which is closely associated with the epithelium.

Histologically, the tumor is composed of irregular clefts and acinar-like space lined by epithelium which is usually tall columnar and pseudostratified. Many of the glands show the bud-like drops that are seen in the epithelium of the apocrine glands. Other groups of cells are ciliated. There may be large, cyst-like spaces lined with flattened epithelium, which contain concretions and granular debris. In other areas the epithelium is of definite papillomatous pattern with projections into the large cystic spaces. Small areas of epithelium may differentiate toward the squamous type. There is a varying amount of lymphoid stroma which is in intimate relation with the epithelium. Secondary follicles are occasionally present.

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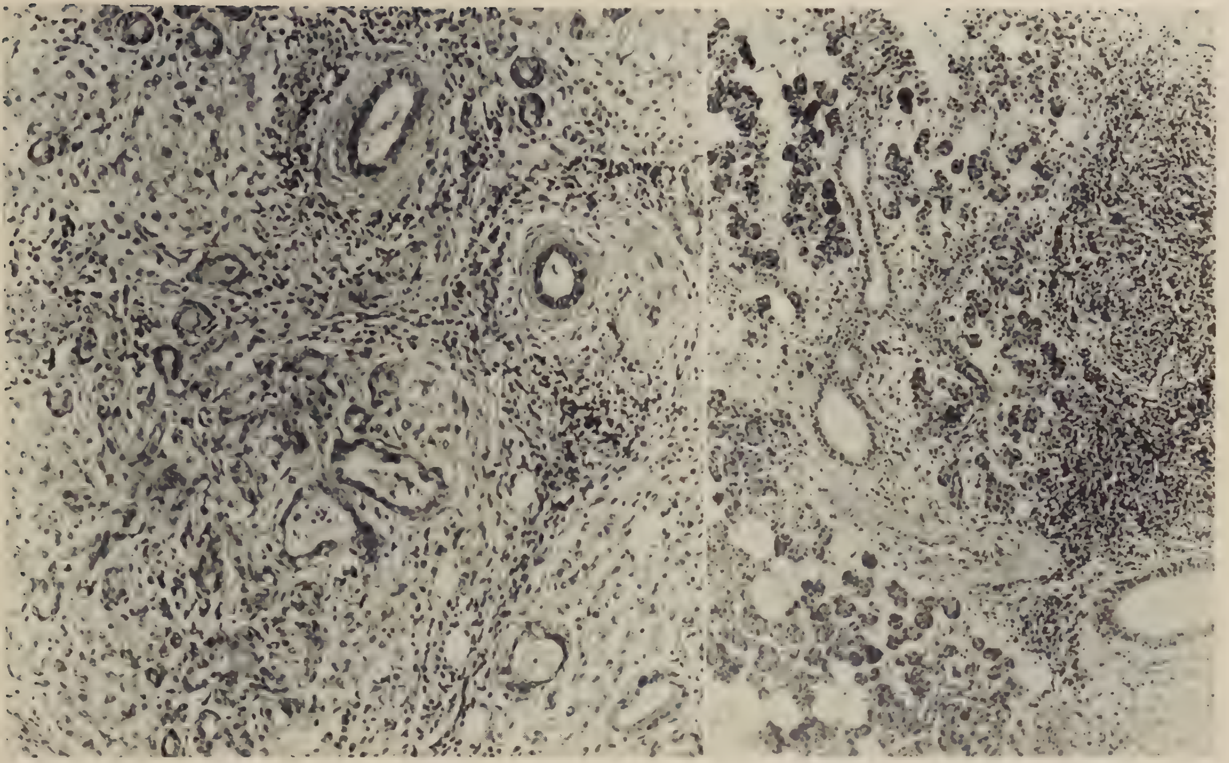
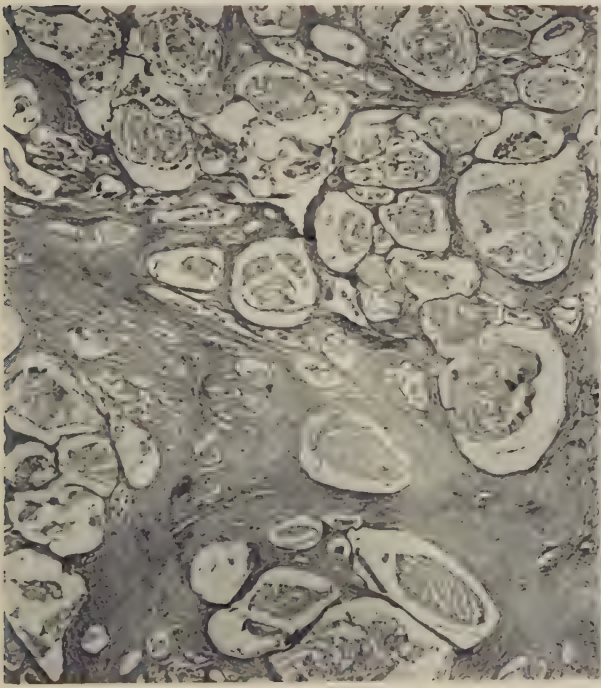
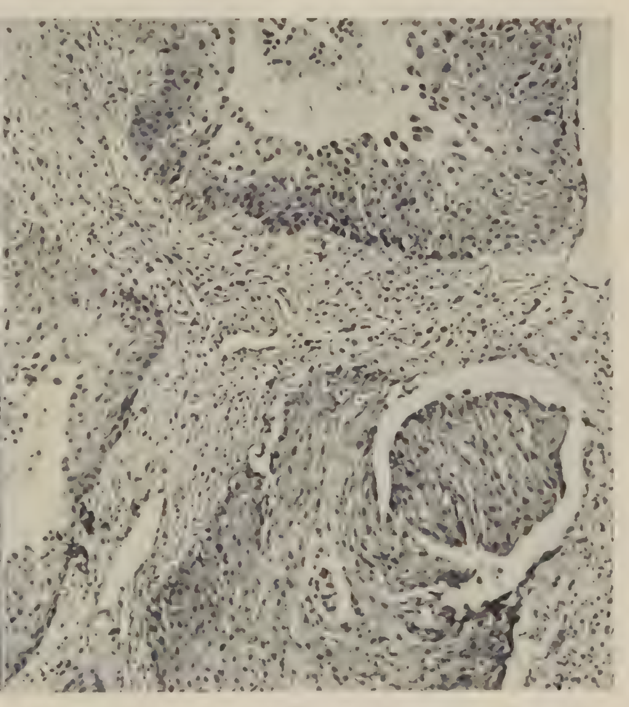
SIALADENITIS



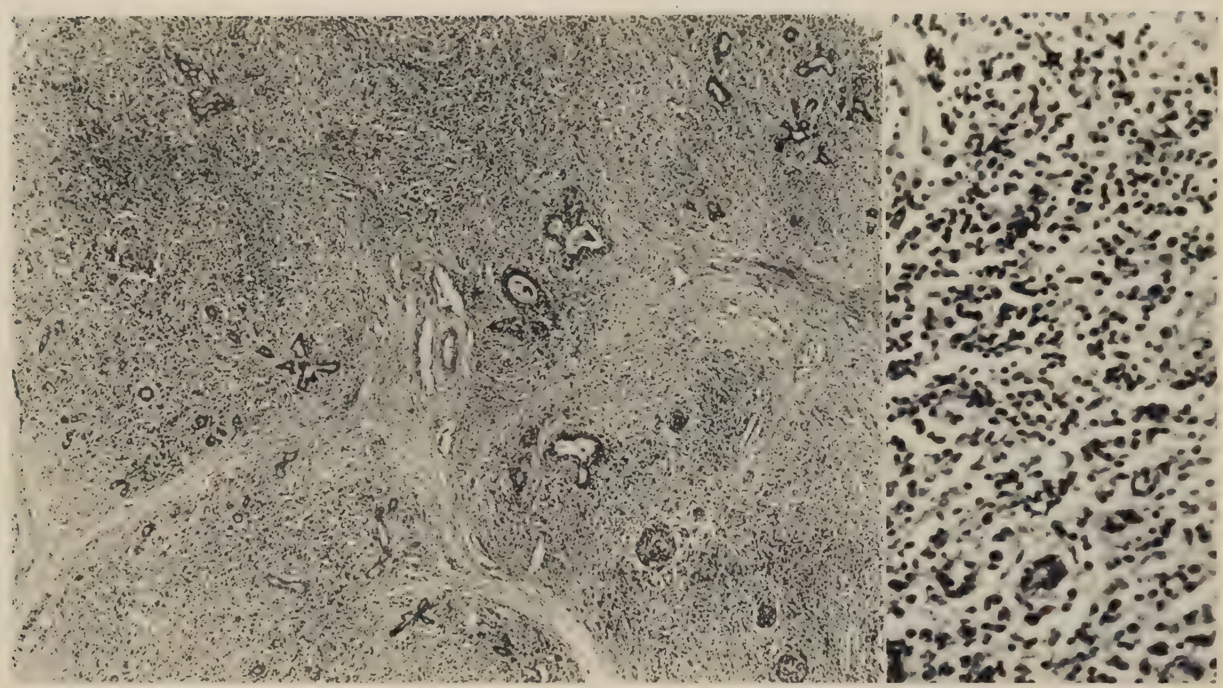
Chronic inflammation and acinar atrophy. Obstruction of salivary gland duct by stone (sialolith), as in this 37 year old man, caused recurrent swelling of the gland and pain, especially on eating. Chronic inflammatory reaction (sialadenitis) with accumulation of exudate, predominantly of mononuclear cells; atrophy of gland acini; fibrosis. x145, x100.



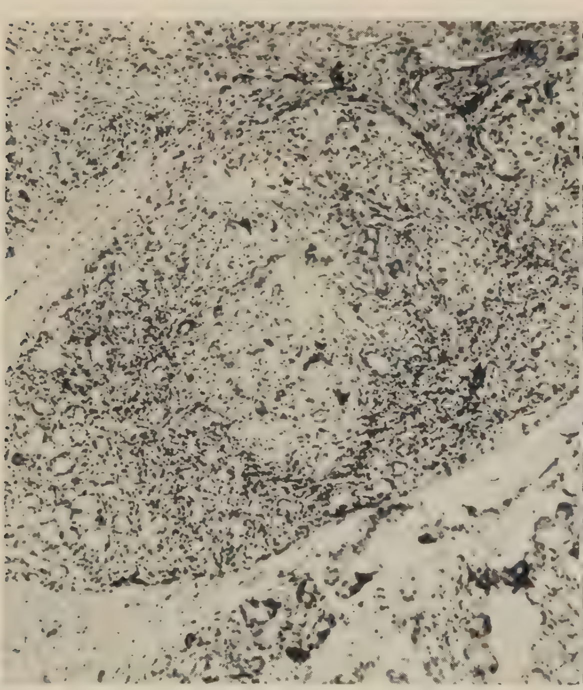
Cystic dilatation and fibrosis. After long-standing occlusion and in the absence of infection, the gland has been reduced to a collection of cysts embedded in scar tissue. Lobular pattern of salivary gland maintained. x21.



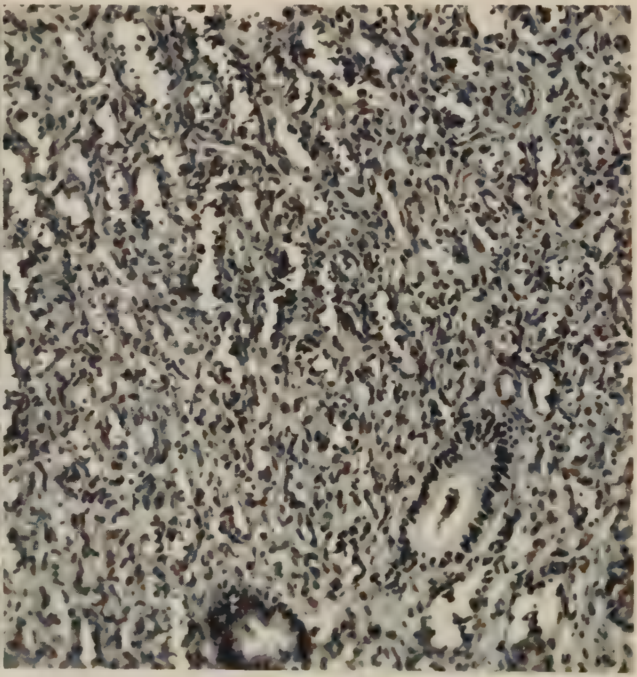
Hyperplasia and metaplasia of ductal epithelium. Occasionally the epithelium of the ducts undergoes squamous metaplasia. In this case it led to the erroneous diagnosis of squamous cell carcinoma. x130.



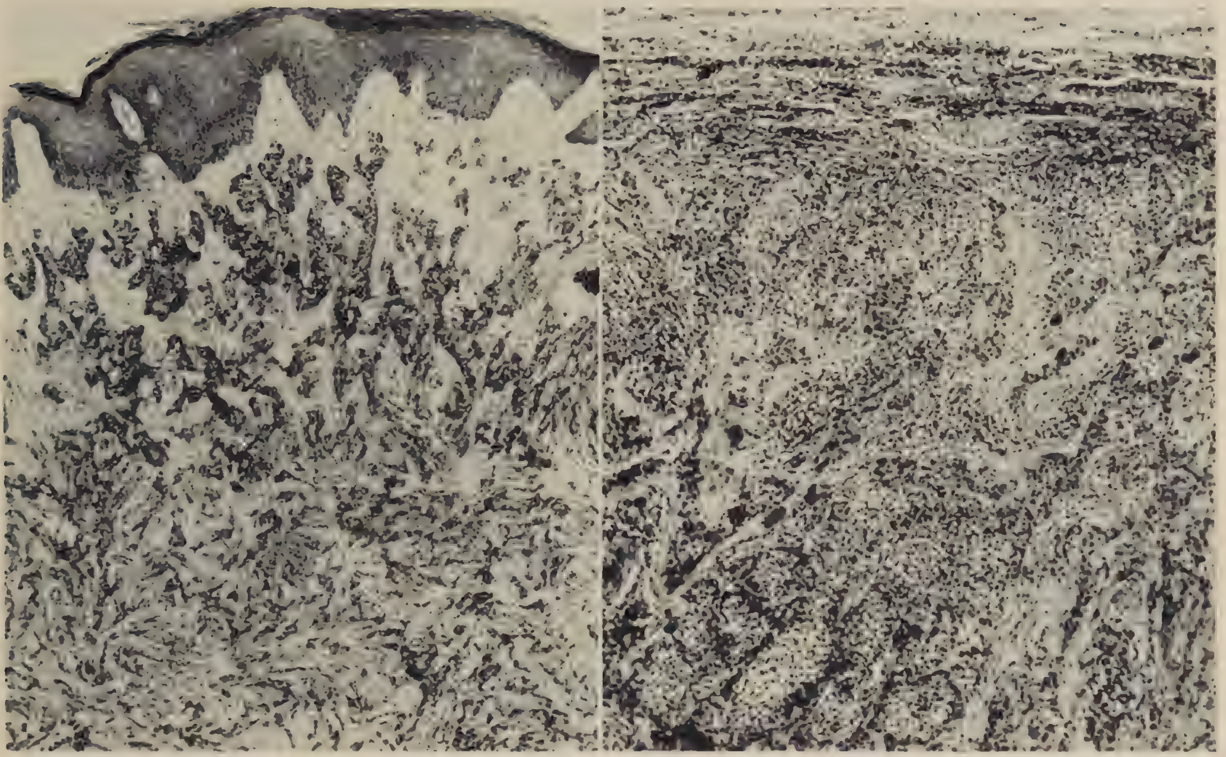
"Benign lymphoepithelial lesion" (adenolymphoma, Mikulicz' disease, chronic inflammation, etc.) of the parotid gland, initially diagnosed Mikulicz' disease. Clinical diagnosis was carcinoma, after the condition had been present for one year in a 51 year old man with no enlargement of other salivary glands or lacrimal glands. Large and small epithelial islands, many of which are ductlike structures, surrounded by apparently normal lymphocytes, the dominant element. Diffuse involvement of entire gland in this case. x40, x320.



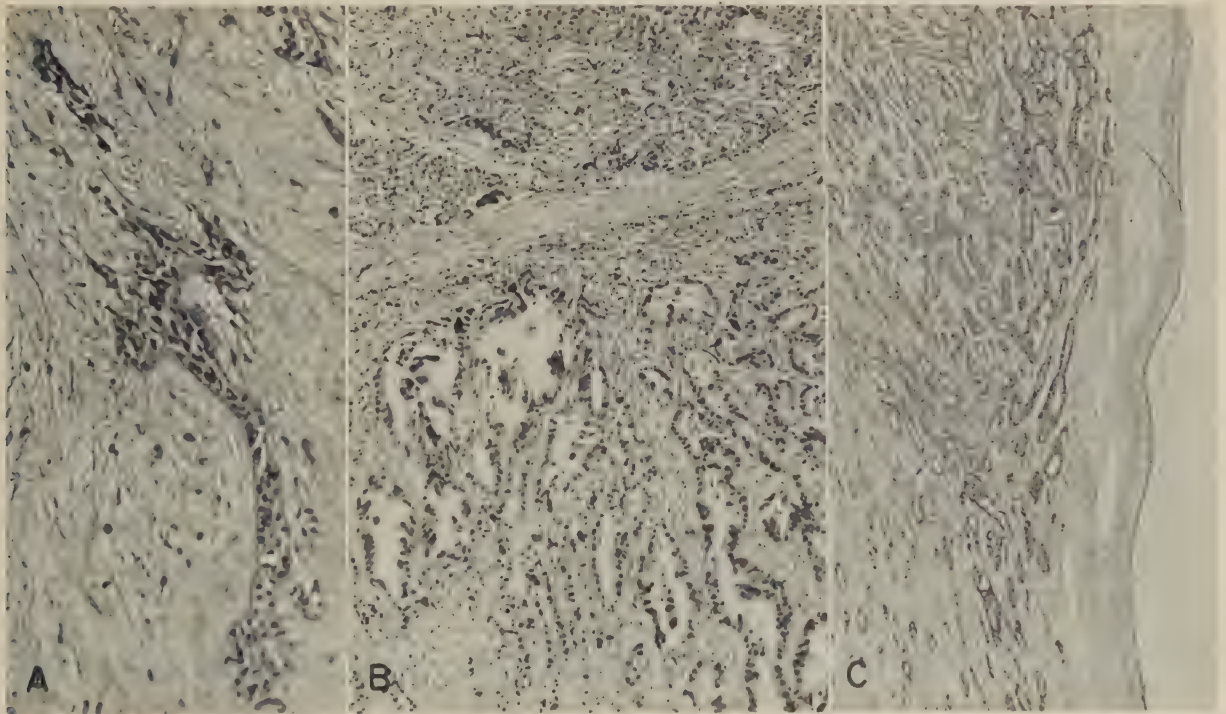
Tuberculosis, submaxillary gland, from a 21 year old woman with pulmonary tuberculosis. Excision because of clinical diagnosis of "cyst." Miliary tubercle in a lobule of the gland. Chronic and granulomatous inflammation; atrophy of glandular parenchyma. x130.



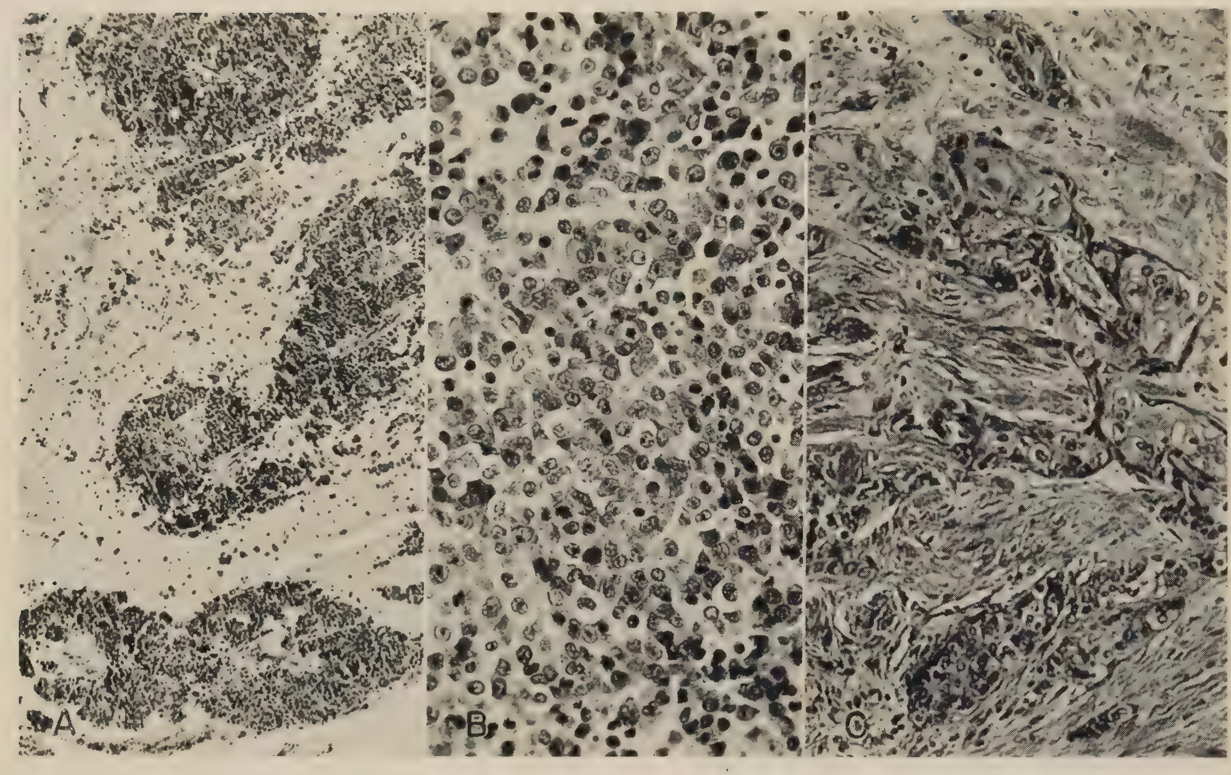
Capillary hemangioma extensively involving parotid gland. 10 month old baby with an ill defined tumor in anterior triangle of neck that could not be completely removed. Mass of capillary blood vessels; two ducts are only evidence of gland lobule. x165. (Youngstown Hospital, Ohio)



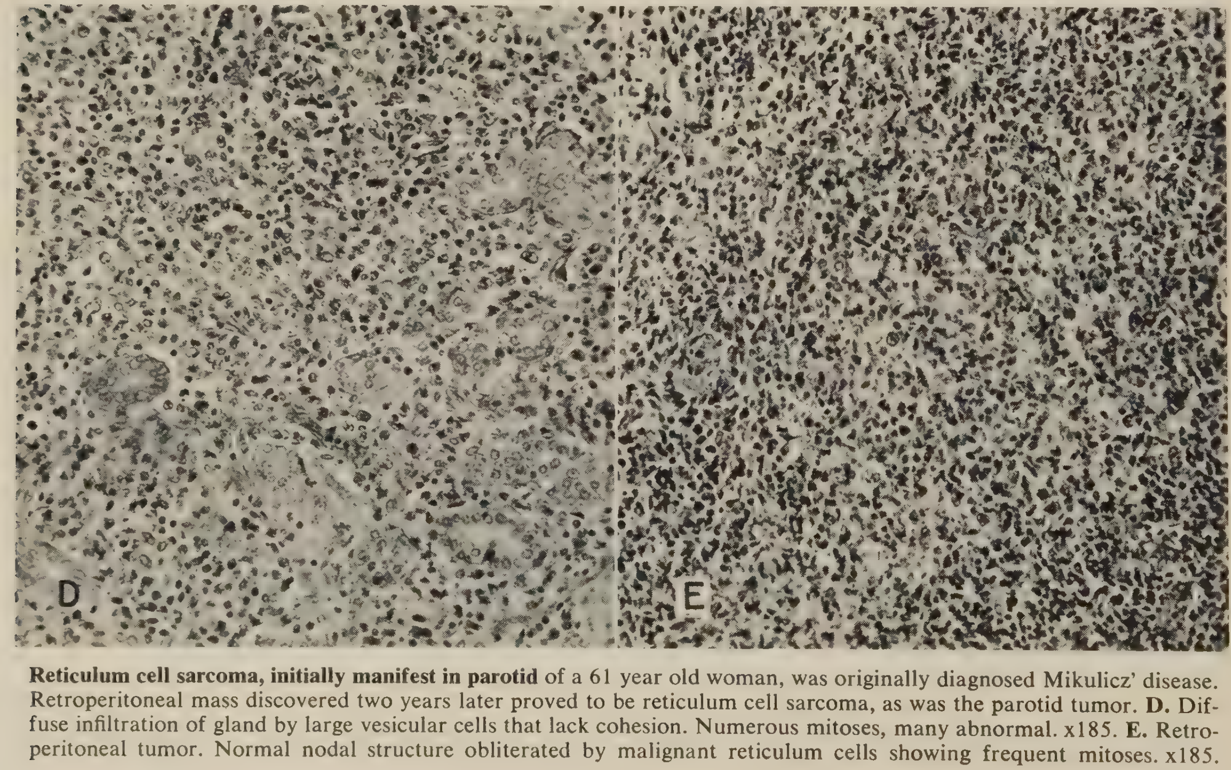
Malignant mixed tumor of "accessory" salivary glands, hard palate. *Left:* surface of unencapsulated mass which contained large areas with appearance of benign mixed tumor. x48. *Right:* metastatic tumor in lymph node. x75.



A. Benign mixed tumor of the parotid which had not recurred two years after removal. x125. **B. Adenocarcinoma,** believed to have arisen in a mixed tumor of submaxillary gland of a 63 year old man, produced generalized metastasis. x76. (E.G. McPherson, Stockbridge, Mich.) **C. Invasion of skin by a parotid tumor** in a 49 year old man. At death, fourteen years after tumor was first noticed, there were metastases to lungs and lymph nodes.



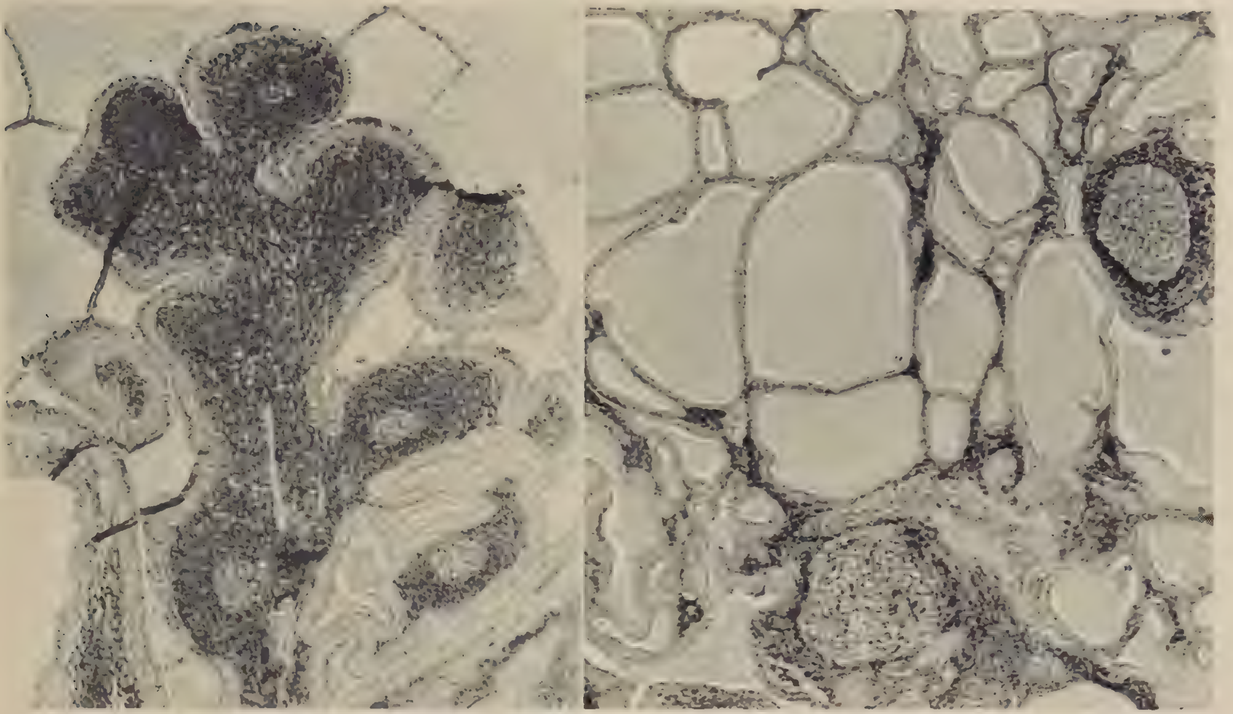
Undifferentiated carcinoma. Infiltrating parotid tumor in 54 year old man grew rapidly involving cervical lymph nodes. Despite radical dissection and irradiation therapy, death occurred seven months after clinical recognition. Extensive local invasion; lung metastases. **A.** Poorly differentiated neoplasm considered "transitional cell" or anaplastic adenocarcinoma. Perivascular arrangement. x76. **B.** Small cells that appear epithelial. x315. **C.** Epidermoid carcinoma in some foci. x137.



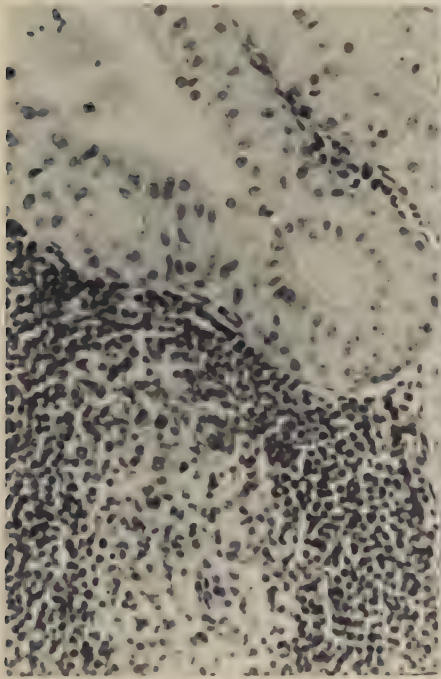
Reticulum cell sarcoma, initially manifest in parotid of a 61 year old woman, was originally diagnosed Mikulicz' disease. Retroperitoneal mass discovered two years later proved to be reticulum cell sarcoma, as was the parotid tumor. **D.** Diffuse infiltration of gland by large vesicular cells that lack cohesion. Numerous mitoses, many abnormal. x185. **E.** Retroperitoneal tumor. Normal nodal structure obliterated by malignant reticulum cells showing frequent mitoses. x185.

PAPILLARY CYSTADENOMA LYMPHOMATOSA

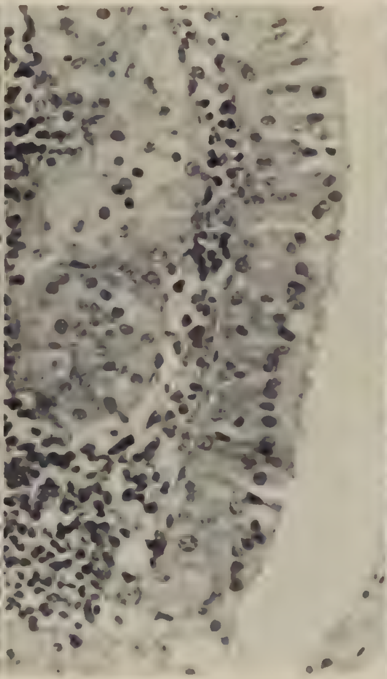
(WARTHIN'S TUMOR)



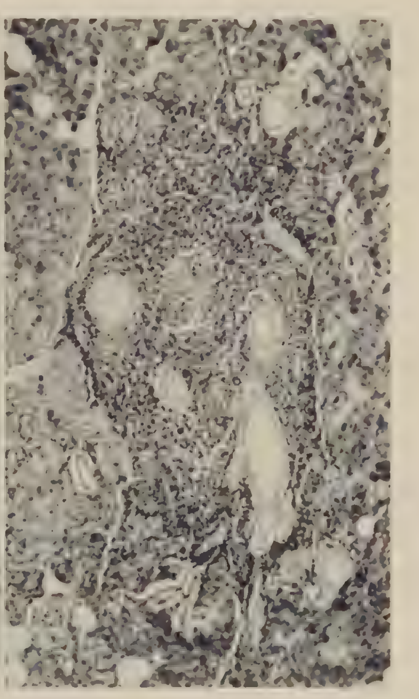
The basic constituents of **Warthin's tumor** are glandular epithelium with intimately associated lymphatic tissue, as seen in this example from angle of jaw of a 46 year old man. A papillary element is common. x 70. Gland acini contain colloid-like material. Note the secondary lymphatic follicles. x 36.



The epithelium is usually of tall columnar type. Note direct contact between epithelium and lymphatic tissue. x 280.



The epithelium is occasionally ciliated. Islands of squamatoid cells may also be found. x 300.



Warthin tumor-like inclusion in salivary gland is incidental finding. Microscopic collections of ducts with closely applied lymphatic tissue. x 60.

CHAPTER 31

EXTERNAL EAR

It is not within the province of this atlas to discuss the details of developmental defects that do not lend themselves to pathologic examination. There are, however, about the external ear congenital fissures and cysts that require excision, particularly when they become infected. They are usually anterior to the ear but occasionally are posterior, and vary from shallow depressions to fistulous tracts that may extend deeply and parallel to the external auditory canal as far as the middle ear. They may be multiple, unilaterally or bilaterally. When there is no orifice, a cyst develops. The lesions are the result of incomplete closure of the first branchial pouch or incomplete fusion of the tubercles from which the external ear develops. They are usually lined by simple squamous epithelium. At times epidermal elements, particularly hair follicles and sebaceous glands, may be included, and in such instances the cyst can be called dermoid. Altmann has recently reviewed the subject of fistulas and other malformations of the auricle and external auditory meatus.

The skin of the auricle, particularly that of the lobulus, and the first portion of the external canal contains numerous hair follicles and sebaceous glands. Sebaceous retention cysts are not uncommon in these locations, and pyogenic infections of the hair follicles produce very painful lesions. The skin of the auricle is closely applied to the perichondrium, particularly anteriorly, and infections and tumors of the skin do not have far to go before involving the perichondrium and the cartilage.

The external ear is susceptible to **frostbite** because the skin is thin, there is very little areolar tissue and it is in such close proximity to the avascular cartilage. With mild exposure the only change to be seen is vascular paralysis after preliminary contraction with blanching, but if the exposure is sustained or is to particularly low temperatures, thrombosis of the vessels is established and can result in gangrene with destruction of portions of the auricle. Individuals who have experienced frostbite are usually sensitized to subsequent exposure to cold, when they suffer considerable pain. Vesication and ulceration of the skin resulting from such exposure are refractory to treatment.

One of the distressing experiences of the war was the incidence of frostbite of the ears, nose, and digits of aviators who, through accident or carelessness were unprotected for long or even short periods from the very low temperatures of high altitudes. Friedman has written comprehensively on the frostbite material received at the Armed Forces Institute of Pathology during the war.

Herpes zoster is a viral disease in which the infection localizes in the spinal ganglia, producing severe pain and accompanied by vesicating skin lesions. It is most common along the course of the intercostal nerves and around the orbit but occasionally the ears are involved. Pain is particularly excruciating in the ear and the mastoid. Vesicles develop on the auricles and in the external auditory canal, usually on the anterior surface of the lobe of the auricle. Disturbances of hearing or vestibular function are frequent. O'Neill believes that involvement of the ear is more common than is suspected because the eruption is so often misdiagnosed as eczema or some other simple skin lesion, and the facial paralysis as Bell's palsy. On the other hand, he considers the syndrome of herpes zoster of the ear, facial paralysis and otalgia, which Hunt insists is always due to involvement of the geniculate ganglion, a possible outcome of involvement of one or more of the several cranial and cervical spinal nerves that supply the ear region.

Traumatic Lesions. – The skin, particularly the lobes, may be involved in KELOID formation as the result of trauma. In dark skinned persons it is not uncommon around the wound pierced in the lobule for earrings.

Another form of traumatic deformity of the ear is the so-called CAULIFLOWER EAR of the boxer and wrestler.This is due to trauma to the cartilages which stimulates the activity of the perichondrium. The reaction is not as aggressive as the keloid and rarely involves the fleshy lobule of the auricle.

HEMATOMA (OTHEMATOMA) may occur spontaneously, but more commonly by direct trauma, as in the pugilist. It may be large, involving the major portion of the auricle. It differs from the tumor of perichondritis in being opaque on transillumination while the latter is translucent.

A specific clinical and pathologic entity, possibly of traumatic etiology, is CHONDRODERMATITIS NODULARIS CHRONICA HELICIS (painful nodule of ear). Circulatory disturbance may also be a causative factor and the history of previous frostbite has been obtained. It was first described by Winkler in 1915 as a condition affecting the cartilage of the helix. A few similar nodules have since been reported on the anthelix. The involvement of the helix is predominantly in the adult male, while the rare lesion of the anthelix is the type seen in women. Shuman and Helwig have completed a study of 100 cases at the Armed Forces Institute of Pathology and found that the lesion may appear at any age after twenty, with the largest percentage in the fifth and sixth decades. Eighty-five lesions were limited to the upper free margin of the helix; six were on the anthelix in a group composed entirely of men. They have proposed the simplified term "chondrodermatitis helicis" as adequately descriptive.

Usually a firm round or oval nodule less than a centimeter in diameter is immovably fixed to the skin and cartilage. The lesion is generally convex, grayish white or translucent, and at the summit a crust may cover a central depressed ulcer, which at times suggests early carcinoma. Pain, either spontaneous or initiated by pressure, is the most common symptom.

The histopathologic aspect of the lesion is highly characteristic and includes nodular hypertrophy of the epidermis; a depressed or ulcerated central area, capped by a hyperkeratotic or parakeratotic scale with or without crust formation; edema, homogenization and fibrinoid necrosis of the dermal collagen; proliferation of granulation tissue surrounding and partially replacing the altered dermis; a varying amount of inflammatory infiltrate, chiefly lymphocytes and plasma cells, and perichondritis with or without degeneration of the auricular cartilage. The most striking and consistent change is degeneration of the dermal collagen which often progresses to dissolution and conversion into amorphous debris. Cystlike spaces may either communicate with the surface ulcer or extend down to the cartilage. Perichondritis is a constant feature and in the affected area the perichondrial connective tissue is thickened and layered, producing a hyalin-like cap where fibrinoid necrosis often occurs. Occasionally the cartilage appears almost normal, but as a rule it is conspicuously altered by swelling of the interstitial ground substance and the chondrocytes. In more advanced lesions cysts and cleft-like spaces cause considerable deformity.

Systemic Conditions Involving the External Ear.—The cartilages of the auricle as well as those of the larynx may become infected during TYPHOID FEVER, and at times they undergo calcification or even ossification. In either instance there is an increased possibility of fracture. They share with the other fibroelastic cartilages in the very rare dystrophy described in Chapter 6 and in the peculiar metabolic disturbance, ochronosis, where deposits of melanin cause them to take on a slaty or purplish hue.

A rare condition involving the cartilage is DIFFUSE CHONDRITIS, first described by Gordon and his colleagues. His patient was a 34-year-old Negress with dyspnea and swelling and tenderness of the knees and ankles. Both eyelids became swollen and painful. Hoarseness indicated the involvement of the larynx. Her ears became boggy and tender with nodular thickenings in the pinnae. The larynx and sternum were tender. Tracheotomy was necessary to relieve stridor. Other joints and the bridge of the nose became involved. She died about four years after onset of symptoms.

Cartilages from the ear, nasal septum, knee and sternum were available for study. All of the specimens showed diffuse degenerative changes in the cartilage with abortive attempts at regeneration. Active inflammation was evident only in the specimen from the trachea. There was considerable collagenous scarring about the cartilage, possibly of the perichondrium which contained chronic inflammatory exudate. A later biopsy from the ear showed proliferation of mesodermal cells resulting in partially fibrocartilaginous and partially osteoid tissue with small areas of mature bone. The condition is possibly related to Reiter's syndrome. The pathologic changes in the nasal septum are illustrated in the section on the nose.

The ear is a common site for the localization of old fashioned GOUT. The deposit of sodium biurate in the cartilages causes the clinically evident tophi which may persist for many years. When tophi are well developed, the overlying skin is shiny and atrophic.

Microscopically, the cartilage is necrotic in areas that contain irregular slits and ovoid spaces that are the sites of the urate deposits. There is usually an associated fibroblastic reaction surrounding the necrotic areas, but there is a surprising paucity of active inflammatory reaction.

Another systemic disease of importance to the otolaryngologist is LEPROSY. The skin of the lobes of the ears is one of the first places to become infiltrated by the lepra cells. This produces a diffuse thickening and elongation and a peculiar induration to palpation. The details of the pathology are given in the general discussion of leprosy in Chapter 13.

Tumors.—The external ear is the seat of several skin tumors more common on other portions of the face, MOLLUSCUM CONTAGIOSUM, the benign basal cell tumor EPITHELIOMA ADENOIDES CYSTICUM, and NEVUS. The most important tumor, however, is CARCINOMA to which the upper border of the helix is particularly susceptible. It may be of the basal cell or the squamous epithelial type. Tumors of both types are most common in adult males and begin as a wart-like lesion or a scabby ulceration. They may persist as such for a number of years before giving evidence of malignancy. The relative frequency of the basal cell and squamous cell tumors varies with the experience of those reporting them. Early and complete surgical removal is indicated because of the ease with which the cartilage is invaded by either tumor. When this occurs even radical amputation may not eradicate the carcinoma. The clinical difference between the two tumors is that the basal cell tumor does not metastasize but the squamous cell tumor usually metastasizes to the preauricular node. While both tumors are sensitive to irradiation, the basal cell type is the more sensitive.

In a recent article Senturia and Marcus have classified diseases of the external ear. Insofar as possible their classification is on an etiologic basis, but there remain a number of common conditions to which no specific etiology can be assigned.

EXTERNAL AUDITORY CANAL

The auditory canal is divided into two parts, the outer cartilaginous and the inner bony. The entire canal is lined by squamous epithelium which is thicker in the cartilaginous portion and becomes thinner as it approaches the fundus. The portion lining the cartilaginous canal differs further from the remainder in containing ceruminal glands, sebaceous glands, and hair follicles.

Mention has already been made of the vulnerability to infection of the robust hair follicles of the outer portion of the canal. This is manifested as a simple furuncle or as a more diffuse and serious cellulitis.

There are three types of dermatitis that affect particularly the lining of the external canal: seborrheic dermatitis, otomycosis, and eczema, especially the bacterial form. It is important that they be differentiated, for, though they resemble each other clinically, each has its specific treatment.

Seborrheic dermatitis of the ear is often associated with involvement of the scalp. It occurs also in other portions of the body that are rich in sebaceous glands, e.g., over the sternum and in the axilla. This extraotic involvement is an aid in diagnosis. In the auditory canal it is a scaly process, the scales usually being large and brawny. There is some redness of the skin and usually a faint yellowish tinge and crust-like accumulations of sebaceous material. Itching is a common symptom.

Microscopically, the picture is not specific and it varies in relation to the duration of the disease and the degree of secondary infection. It resembles psoriasis rather closely, with parakeratosis, acanthosis of the rete pegs and a moderate inflammatory reaction in the papillae of the dermis. Differentiating features are moderate intracellular and intercellular edema, keratotic scales, and a polymorphonuclear content in the exudate. In spite of its clinical association with the sebaceous glands, the latter show no significant change and there is no appreciable increase in fat content of the dermis or epidermis. Bacterial infection gives an eczematoid character to both the clinical and histologic pictures. There is vesication of the prickle cell layer and an increase in the polymorphonuclear neutrophils. Under these circumstances it is almost impossible to distinguish, either clinically or microscopically, from bacterial eczema.

Otomycosis is far less common than formerly believed, except in warm humid climates. It is characterized by a scaly membranous reaction. While usually more moist and exudative than seborrheic dermatitis, it may be dry. Scrapings from the canal examined in 10 per cent sodium hydroxide solution will reveal the presence of mycelia and spores. There are several species of fungi that can cause the condition but the commonest is *Aspergillus*.

Clinically, itching and pain are usually more prominent than in seborrhea, and the canal becomes plugged by the accumulation of mycelia and exfoliated debris from the ulcerated surface. Secondary bacterial infection is more likely to cause folliculitis and ulceration. Habitual swimmers are plagued by otomycosis; in fact, poorly conducted swimming pools are ready sources of dissemination of the infection.

Microscopically the lining of the canal is swollen from congestion, mononuclear exudate, and edema. The epithelium and superficial layers of the tissue undergo varying degrees of necrosis. The significant feature is the presence of large numbers of mycelia in the superficial layers, enmeshing cells of the exudate. The mycelia do not penetrate deeply into the tissues although they invade below the necrotic surface. The exact identity of the fungus cannot be determined by direct examination but only by cultures on special media. The mere finding of fungus in the ear does not necessarily establish a diagnosis of otomycosis. Fungi can be saprophitic invaders of an eczematous process.

Bacterial eczema is the commonest form of otitis externa. It was very troublesome during the war, particularly in the Southwest Pacific theaters. Clinically it is readily confused with otomycosis, especially when the latter becomes secondarily infected and takes on an eczematous character.

Senturia studied a great number of cases of otitis externa among Air Corps personnel and found that bacterial infections were the most common cause of the eczematous lesions, *Pseudomona aeruginosa (B. pyocyaneus)* being the organism usually incriminated. Similar observations were made in other military personnel and in all theaters.

Otitis externa hemorrhagica.—Occasionally in the presence of otitis media, especially complicating grippe and influenza, small hemorrhages develop in the skin lining the wall of the canal and may cause considerable pain. They usually disappear within a week or so and leave no residuum.

Aerotitis externa.—Senturia and Peugnet were the first to describe the peculiar reaction in the external auditory canal in aviators who made rapid ascents and descents while wearing inaccurately perforated ear plugs. The external canals became hyperemic and petechiae appeared not only on the linings of the canal but also in the tympanic membrane. At times there were large focal hemorrhages seen as dark bullae that caused the lining to bulge. A closed chamber is formed between the improperly perforated ear plug and the tympanic membrane in which the conditions relative to changes in atmospheric pressure are comparable to those in the middle ear when the eustachian tube is occluded.

Tumors.—Tumors arising primarily in the external auditory canal are not common. The TUMOR OF THE CERUMINAL GLANDS has been the subject of considerable controversy. It has usually been reported in the literature as adenocarcinoma, but evidence has accumulated to show that in most instances it is clinically benign. It is a fairly common tumor in cats and dogs, especially the latter, and in these species also it is generally benign. Of the several specimens, human and animal, in the Registry, none has proved malignant. The first case was contributed by Dr. S. S. Hall of Clarksburg, West Virginia. A 45-year-old white woman had noticed the growth in the auditory canal for four years. It was removed in one mass by blunt dissection and was 8 cm. long. This tumor was originally diagnosed as adenocarcinoma. There had been no recurrence after ten years.

The tumor arises either from the ceruminal glands *per se*, or, what seems more likely, from their embryonal anlage. The general pattern of the tumor is adenomatous, made up of acini of varying sizes and shapes, usually lined by pseudostratified columnar epithelium of the apocrine type. Such glands secrete by discharging buds of the protoplasm from the surface of the cells. The epithelium is generally well differentiated and the glandular pattern in most areas is distinct, but in addition there are sheets and strands of cells that do not show the specialization of those making up the acini and there may be areas of differentiation toward the squamous type of cell. The tumors grow expansively rather than by infiltrating aggressively. They fill the canal and project through the external orifice. Histologic evidence of invasion, however, is usually seen, as in the case reported by Warren and Gates and in the cat and dog tumors. It is not surprising, therefore, that these tumors are not infrequently diagnosed as adenocarcinomas. Lukens reported as adenocarcinoma a large red growth that was attached to the floor of the canal and protruded from the ear. He removed it by operation and irradiation and there was no recurrence at the end of seven years.

The cell pattern is definitely more complicated than that of the nonceruminal gland tumor. It resembles rather closely the gland elements seen in papillary cystadenoma lymphomatosum occurring in the region of the parotid gland. The lymphatic tissue element, however, is not seen in the ceruminal tumor.

HEMANGIOMA of the external canal is not rare, and OSTEOMA is relatively common. Both of these tumors are benign. Osteomas generally arise at the osteocartilaginous junction of the canal and are considered by some as exostoses rather than tumors. Such bony overgrowths have a racial incidence and intrinsic factors undoubtedly influence their occurrence. They develop in late adolescence or early adult life, most commonly in males. Mechanical or chemical irritation also play a part in their formation. Van Gilse postulated a causative effect of exposure to cold water, for he observed exostoses in the auditory canals of persons who habitually swam in cold water but not of those who swam in warm water. Confirmation of his view was furnished by the experiments of Fowler and Osmun, who caused overgrowths of bone in the ears of guinea pigs by injecting cold water.

Ruttin called attention to the relative frequency of exostoses about the external margin of the annulus.

CARCINOMAS, both basal cell and squamous cell, occasionally develop in the epithelium of the canal, the basal cell type most commonly near the external orifice. This is a particularly dangerous place, for invasion of the cartilages of the part makes surgical removal difficult.

One instance of CHONDROSARCOMA apparently arising from the cartilaginous portion of the canal is in the Registry. This is from a five-year-old colored boy who entered the hospital with a polypoid lesion in the canal. It was removed but recurred in a few weeks and later developed into a large subcutaneous mass that choked the canal and caused considerable protrusion of the external ear. It extended down into the neck but did not metastasize. The patient died five months after the initial removal.

Otic polyp.—This lesion is included in the discussion of the external auditory canal because that is where it is most evident clinically. It has its origin, however, in the middle ear, as a complication of chronic otitis media. Of 21 cases in the Registry, 19 had a history of middle ear disease of four to twenty-two years' duration. The polyp is essentially a mass of granulation tissue exhibiting a certain amount of neoplastic aggressiveness. It reaches the external canal through an ulcerated tympanic membrane and arises most commonly from the mucosa over the bony labyrinth. Only occasionally does it seem to arise from the external canal, and then from the upper recess between the canal wall and the tympanic membrane. Such a polyp is a result of chronic inflammation in the attic.

The polyp has been given a number of specific names based on its varying histologic character —

adenomatous, cystic, fibrous, and granulation tissue, for example. There is no indication, however, that it is other than the result of chronic inflammation, and it is somewhat comparable to the nasal polyp, except that it is rarely so edematous. It is covered by the columnar epithelium of the middle ear, or occasionally by metaplastic squamous epithelium. Ulceration is common. The body of the polyp is made up of granulation tissue, i.e., abundantly vascularized young connective tissue in which there is a varying amount of chronic inflammatory exudate. As a result of ulceration, there may be secondary infection with a higher content of polymorphonuclear leukocytes. At times, included in the body of the polyp are mucus-secreting glands, giving the tumor a cystic character if they are distended by retained secretion. Other polyps may show cholesteatomatous cysts arising from included squamous epithelium.

Hyperplasia of the covering squamous epithelium that may simulate carcinoma has been described, but there is no instance in the Registry of actual malignant change in this lesion.

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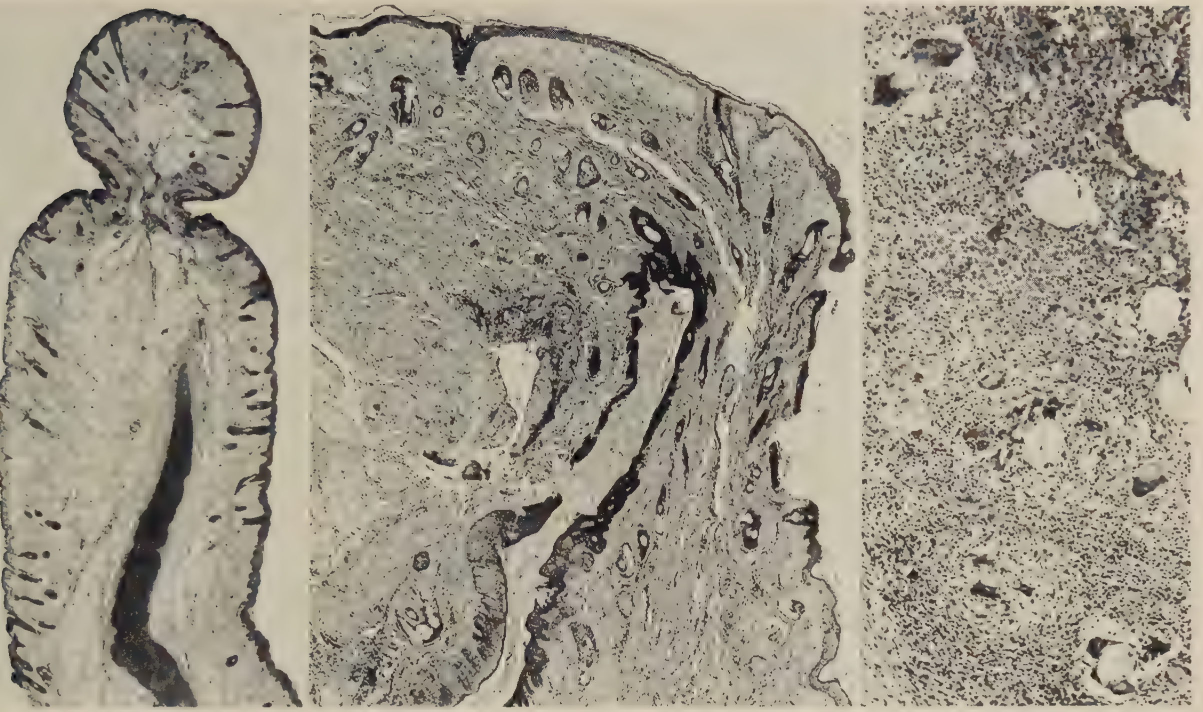
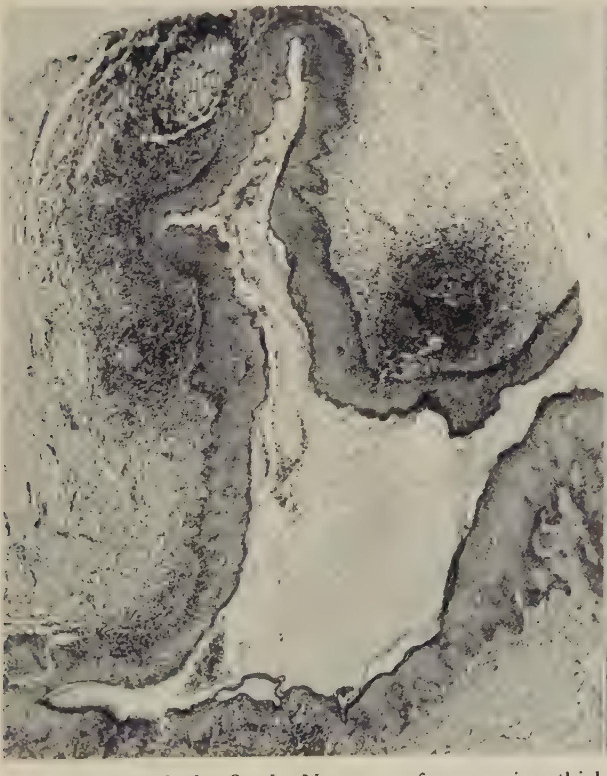
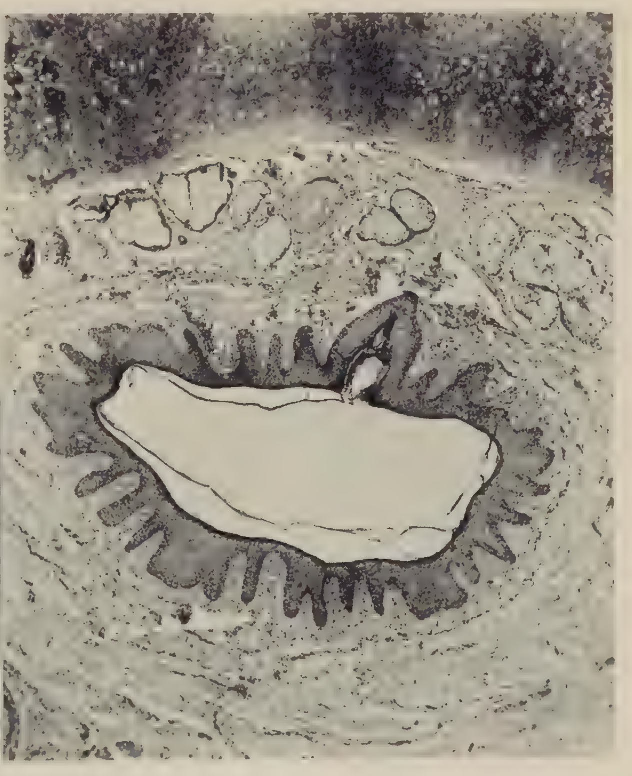


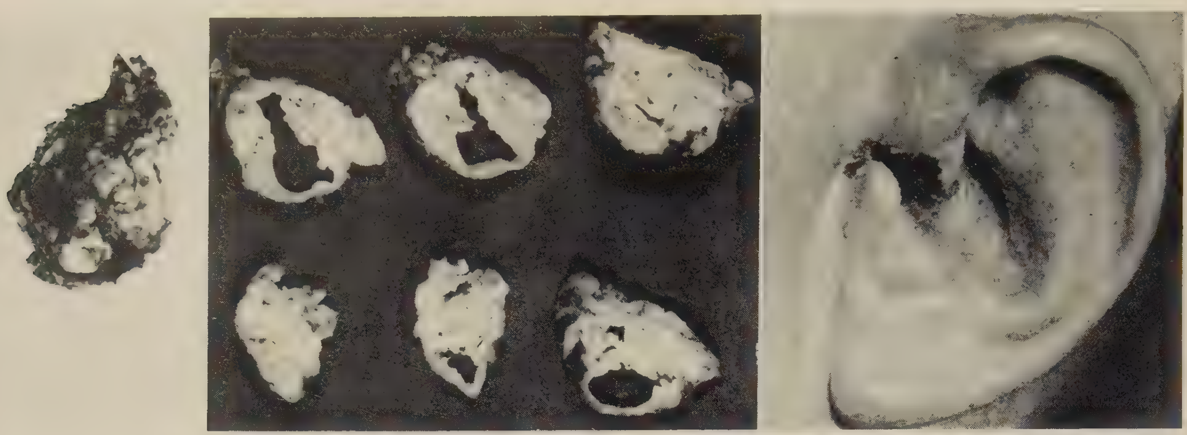
A. Accessory ear, attributable to maldevelopment in early fetal life, from a 3 month old infant. x 13. B. **Auricular** fistula, result of inclusion from first branchial cleft, lined by squamous epithelium. Healing depends on complete removal of inclusion. x 27. C. Deep portion of congenital auricular fistula from a 3 year old child. "Extra lobe" on right ear, present at birth, showed a periodic purulent discharge. Foreign body granulomatous reaction to keratin in addition to pyogenic inflammation. x 75.



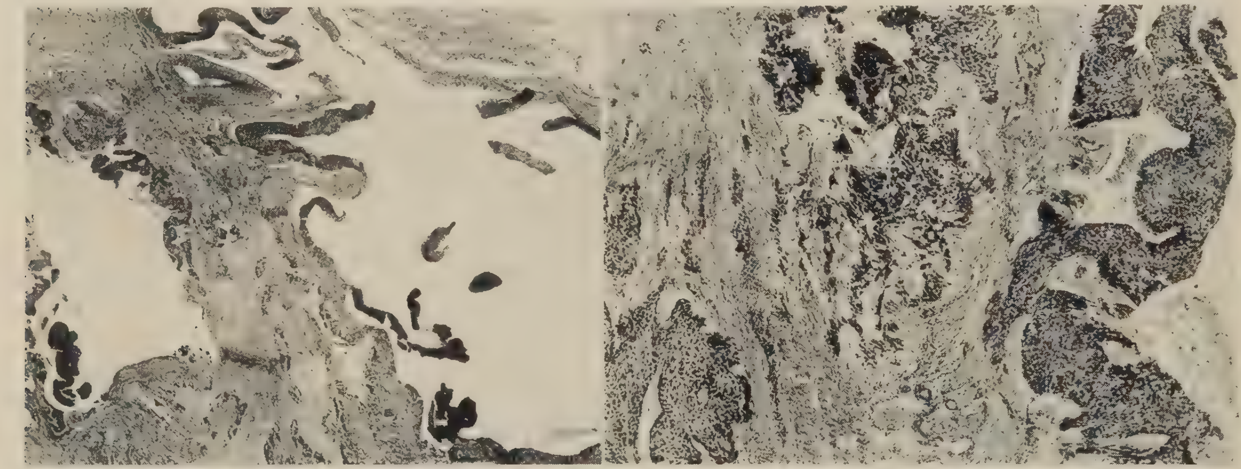
Congenital auricular fistula. Narrow surface opening; thick squamous epithelial lining; severe inflammatory reaction in deeper portions. x 48.



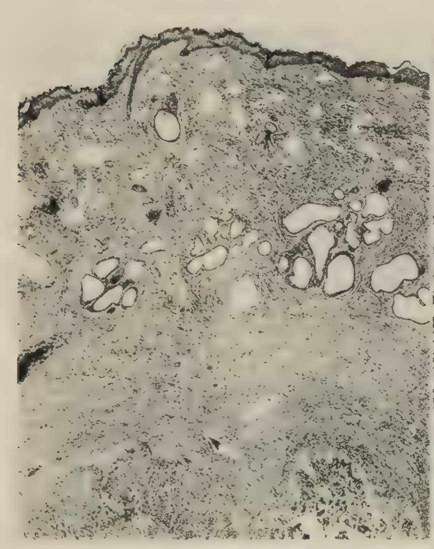
Congenital auricular fistula; cross section, including cartilage of pinna. Note the sebaceous glands. x 48.



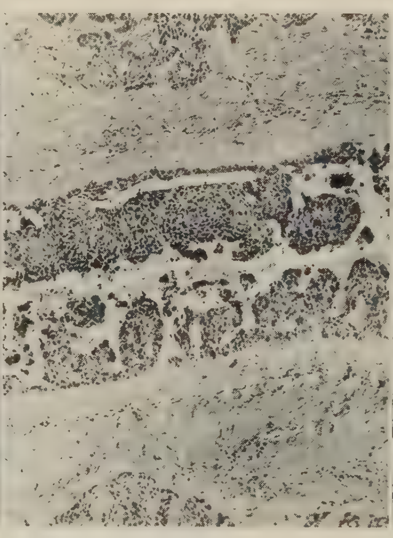
Small subcutaneous tumor under a dimple in the skin, just anterior to ear. Apparently a relic of first branchial cleft. Actual size of surgical specimen (left). Cross sections of tumor showing cyst (center). Postoperative appearance of ear (right).



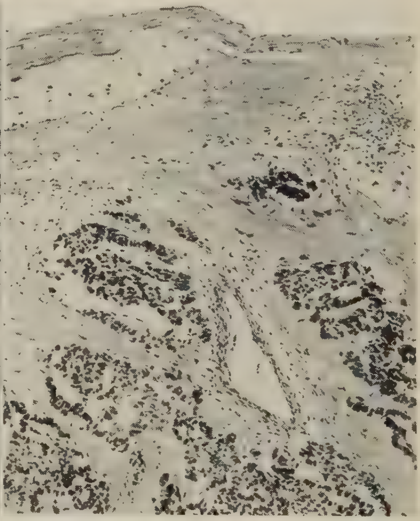
The cyst is lined by squamatoid epithelium, clearly neoplastic at higher magnification. Basaloid cells are infiltrating the deeper tissue. x 8, x 55.



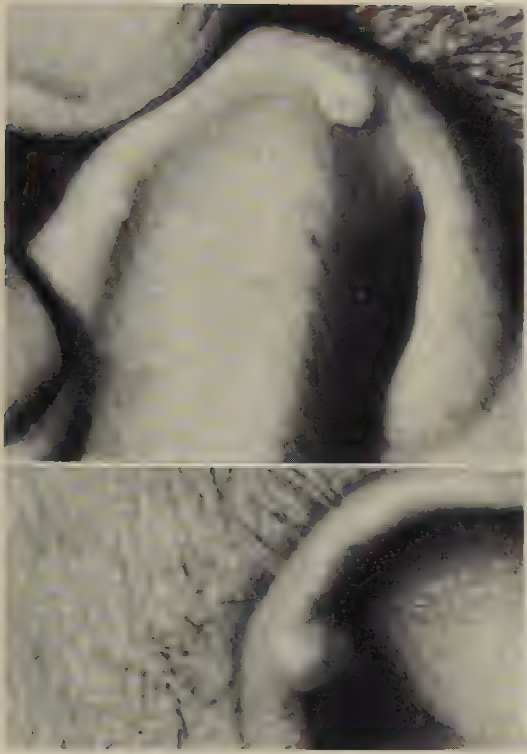
Tumor advancing from below toward surface of external canal. x 27.



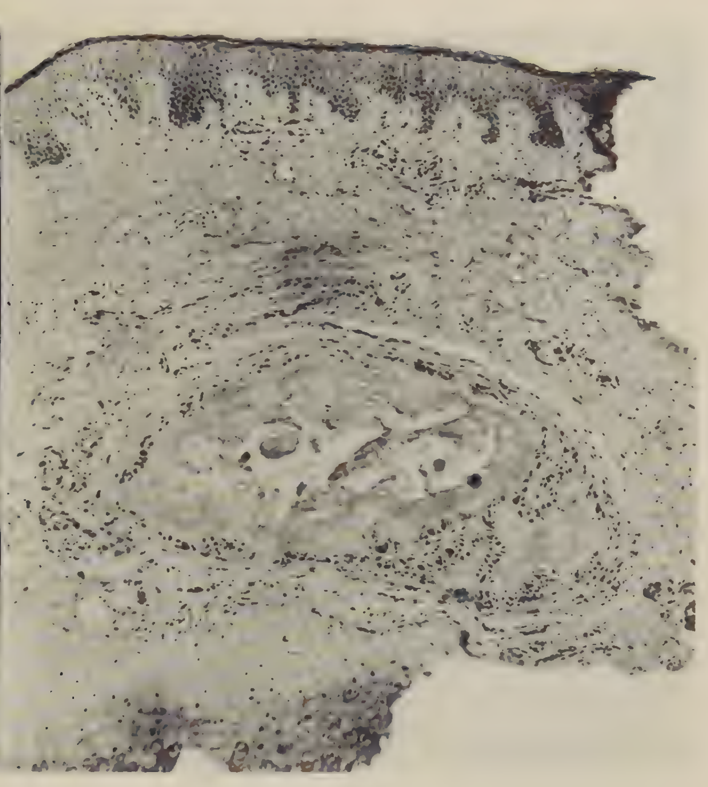
Invading tumor removed by radical resection four years after primary removal. Intensive irradiation and surgery failed to halt its progress. x 55.



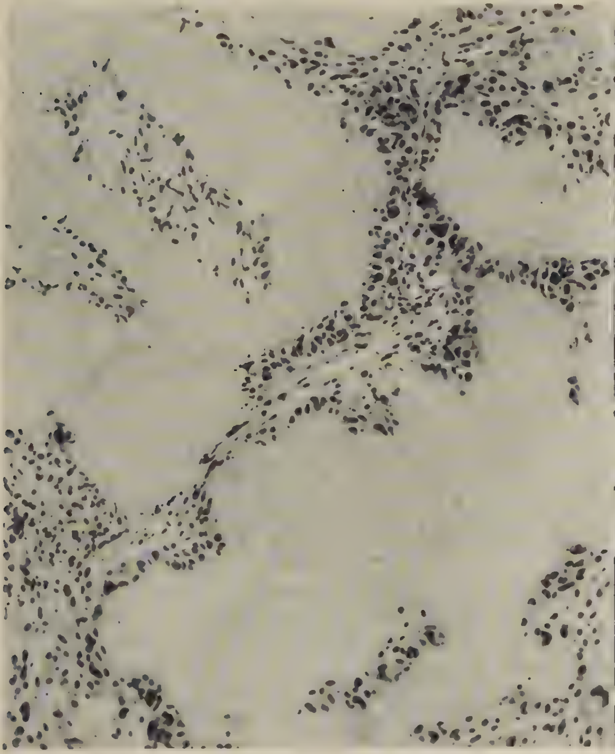
Tumor found in dura at autopsy, seven years after onset. It is basal cell carcinoma. x 70.



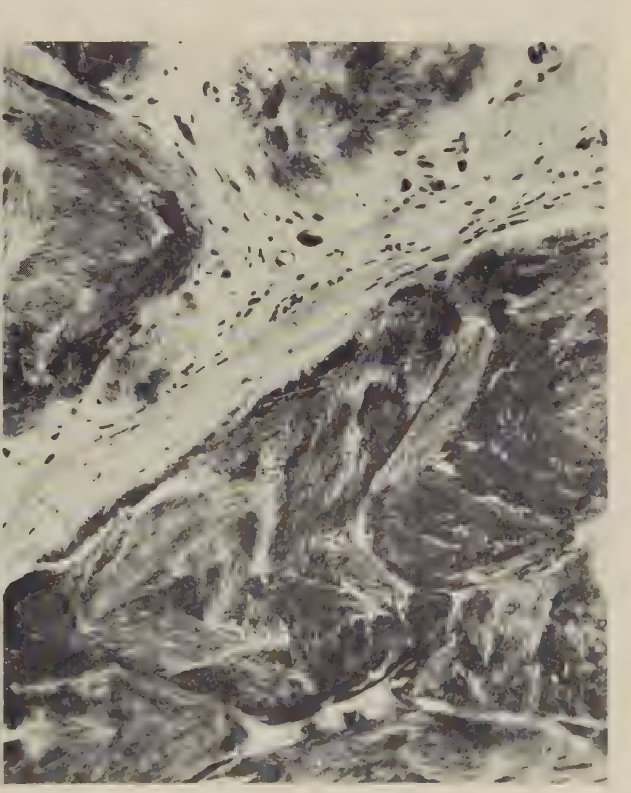
Two examples of the clinical gouty tophus. It could be confused with the preulcerative phase of chondrodermatitis nodularis chronica helicis.



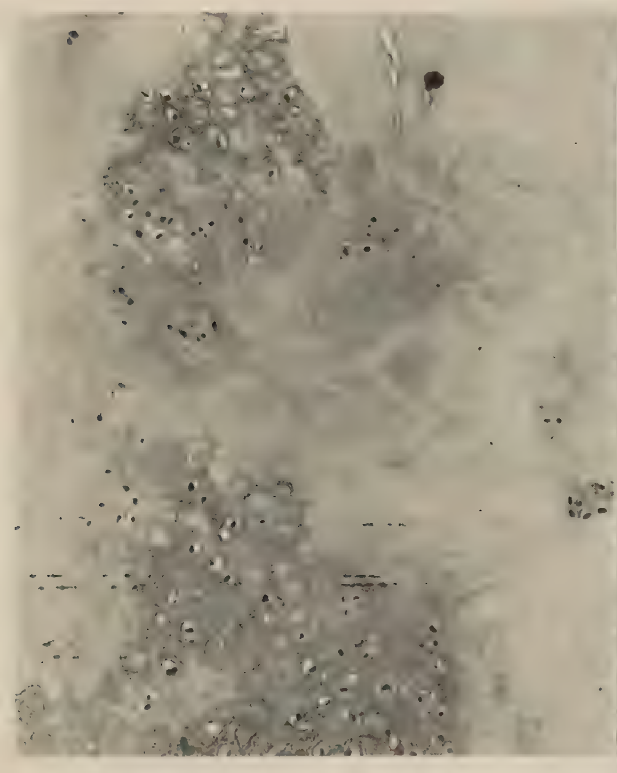
Collection of crystals circumscribed by fibrous tissue deep in dermis near cartilage. x 76.



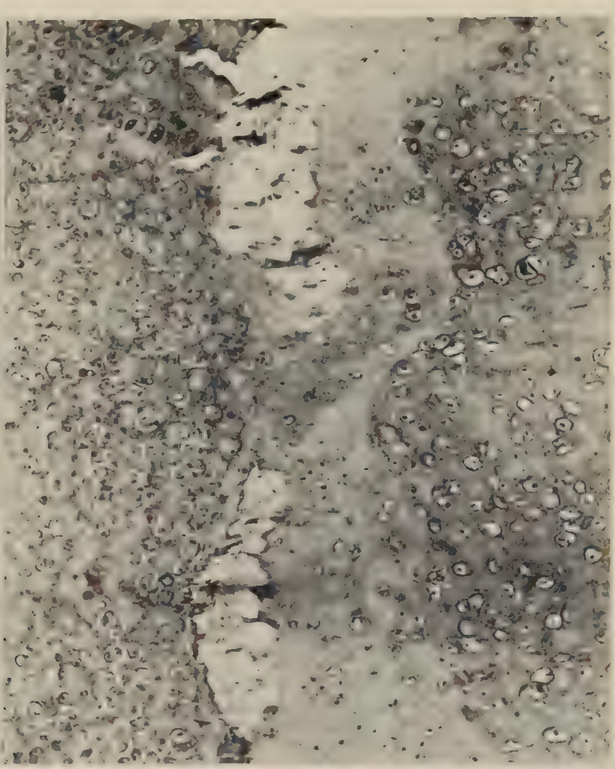
Amorphous masses surrounded by epithelioid cells and fibroblasts. There is remarkably little inflammatory reaction. x 125.



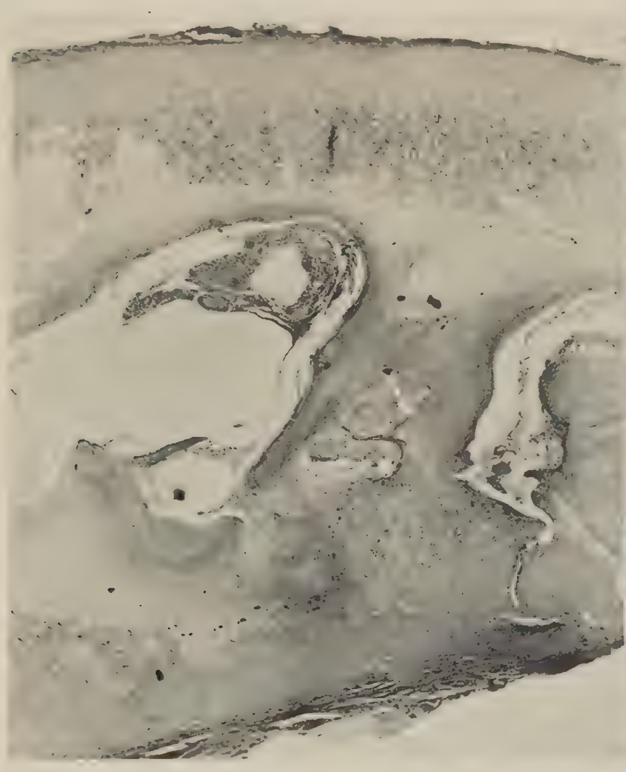
Compact masses of undissolved crystals in centers of quiescent lesions. x 125.



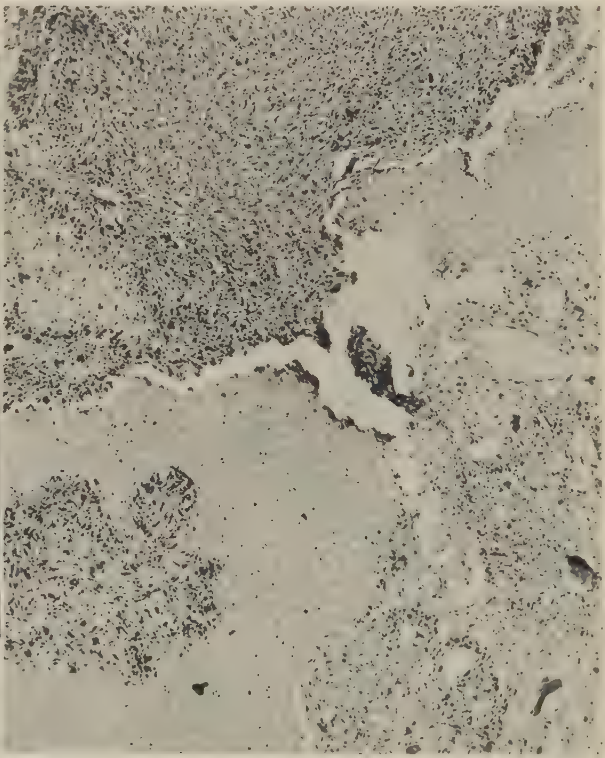
Bland homogenization with loss of chondrocytes; diagnosed chondroma. x 125.



Cystic liquefaction; reduction in chondrocytes with marked increase in surrounding cartilage, from pinna. x 75.

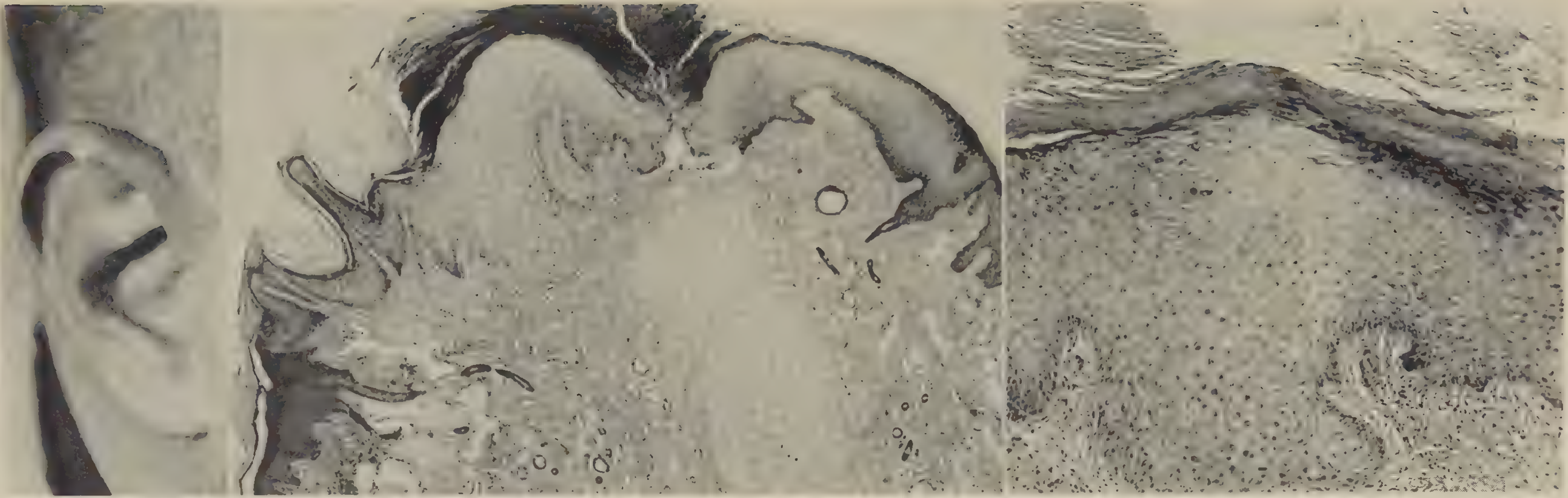


Chondromalacia. Another example of cystic degeneration in more advanced stage. x 48.

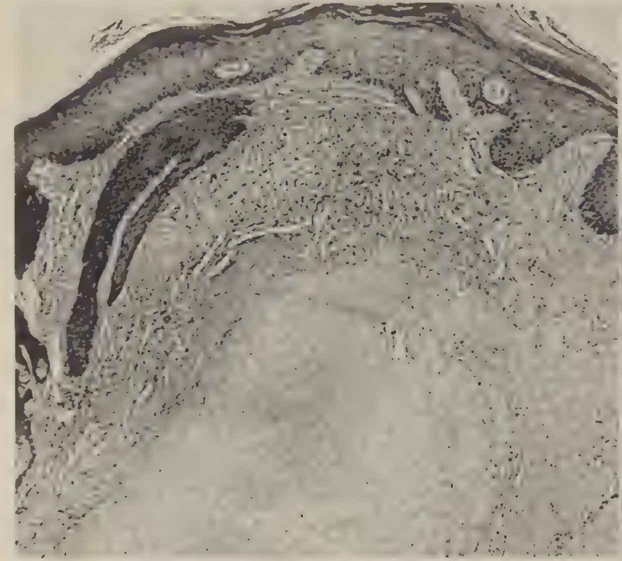


Marked cellular reaction, including foreign body giant cells, to necrotic cartilage. This was diagnosed chondrosarcoma.

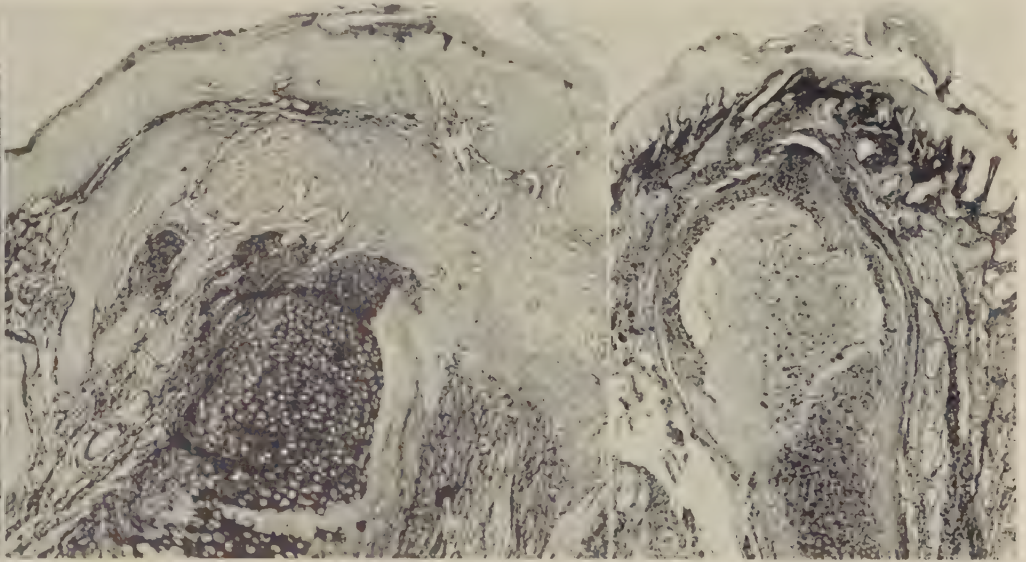
The cartilage of the ear undergoes degeneration and necrosis under a variety of circumstances. The etiology is not always evident.



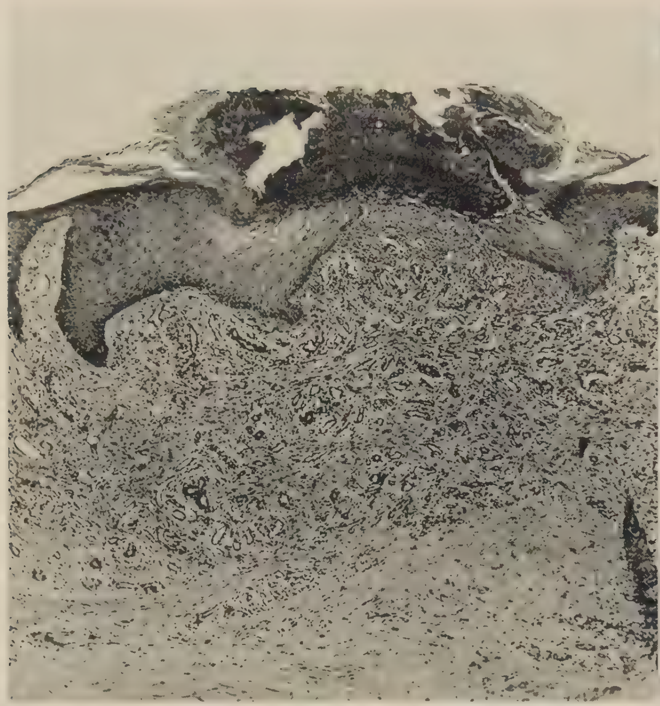
Chondrodermatitis nodularis chronica helicis. Typical site and clinical appearance of early lesion, in this case, bilateral. Acanthotic and hyperkeratotic epithelium; dilated superficial vessels; inflammatory reaction extending from skin to cartilage with cyst formation. x 31. Acanthotic epithelium, at times mistaken for carcinoma. x 55.



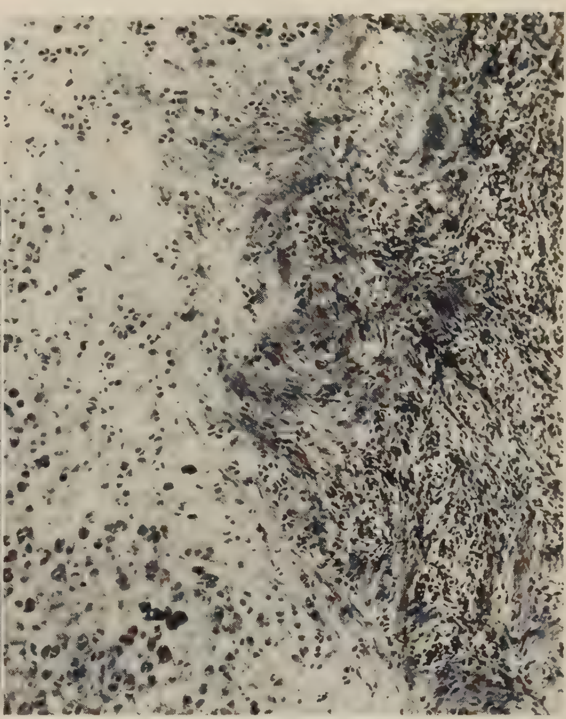
Exudate has invaded perichondrium and the cartilage is undergoing necrosis. x 48.



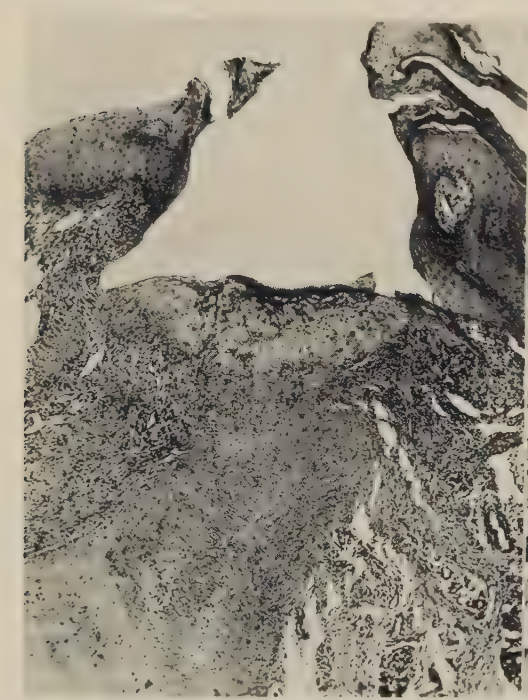
Special stains shows loss of elastica in involved dermis at top; elastica still present (black fibres) laterally. x 48. Epidermis closely applied to cystic cartilage. x 21.



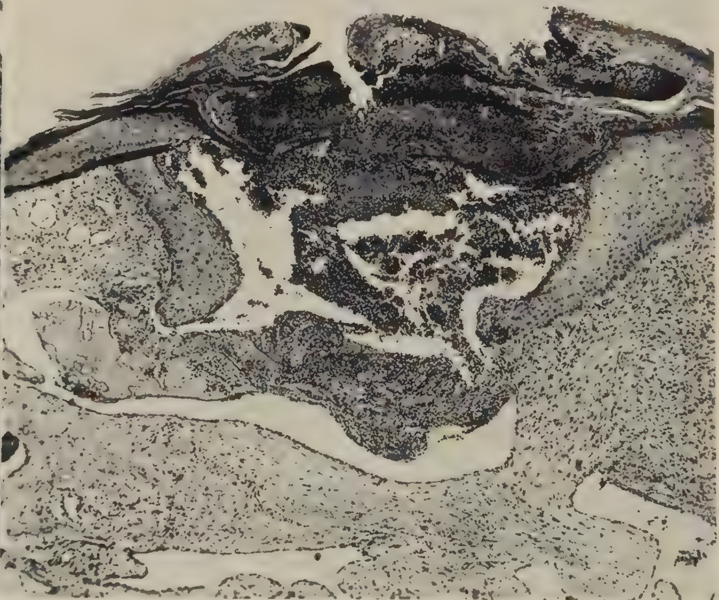
Very vascular granulation tissue reaction, replacing dermis. Crust of necrotic debris on surface. x 48.



The inflammatory reaction has invaded perichondrium. Its outlines are poorly defined. x 114.

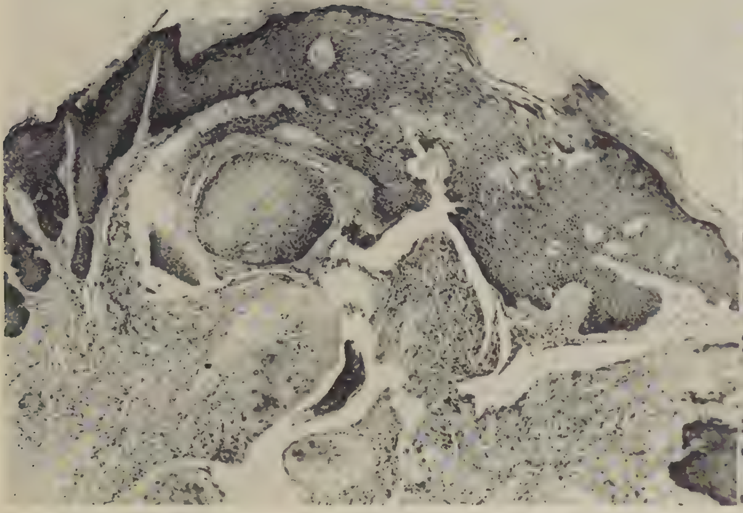


The surface is broken by rupture of cyst and fragment of cartilage is presenting. Perichondrium is badly frayed. x 48.

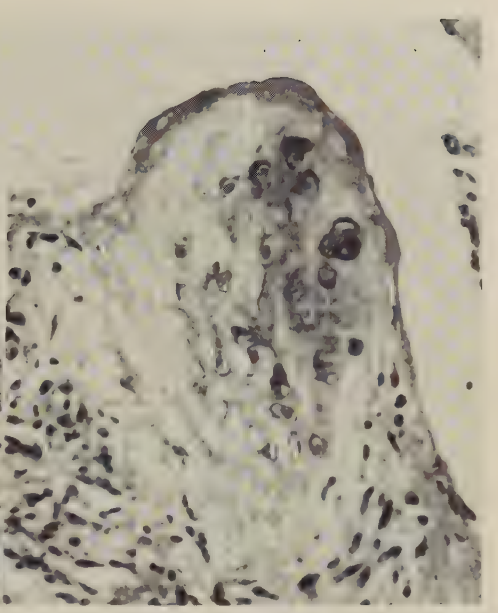


Cyst, filled with necrotic debris and covered by scab, has a fragment of cartilage for a base. Note very wide vascular spaces. x 48.

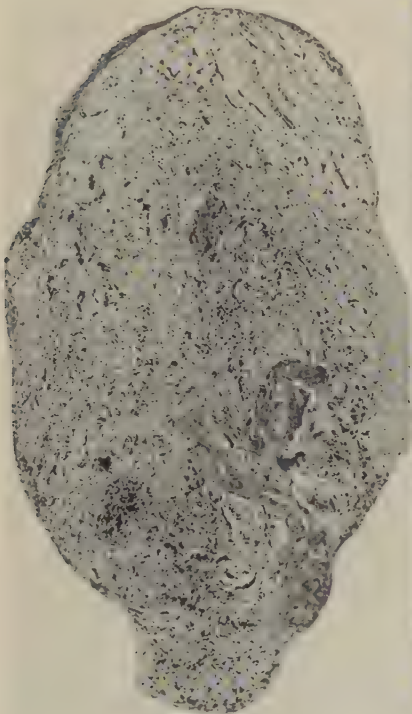
PERICHONDRITIS-DIFFUSE CHONDRITIS



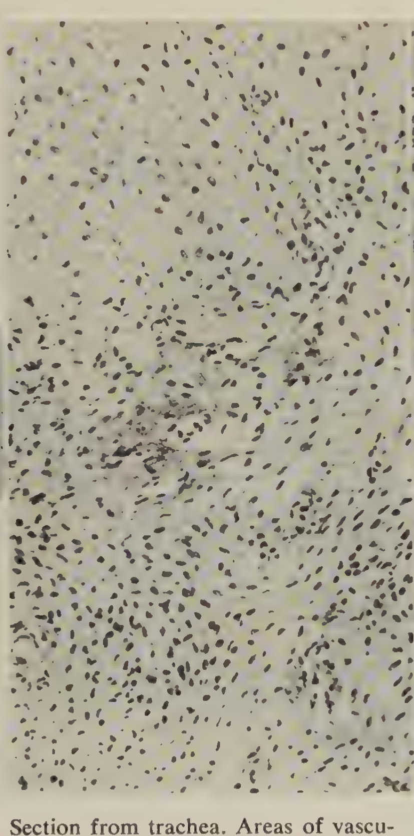
Perichondritis of long standing. Acanthotic epithelium, cystic space beneath; fragmentation of cartilage; dermis replaced by granulation tissue. x 48. Persistent destruction of cartilage results in deformity.



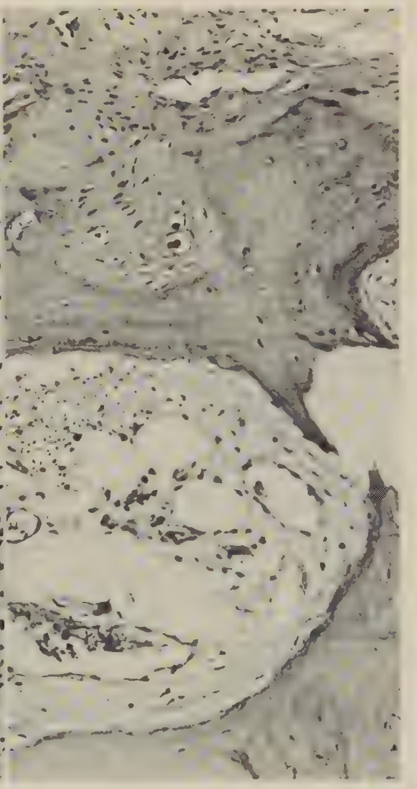
Fragment of sequestrated cartilage partially surrounded by granulation tissue. x 185. Such fragments may be extruded.



Diffuse chondrodystrophy:
Biopsy from ear. Cartilage disrupted by edema, fibrotic tissue, and increased vascularity. x 40.

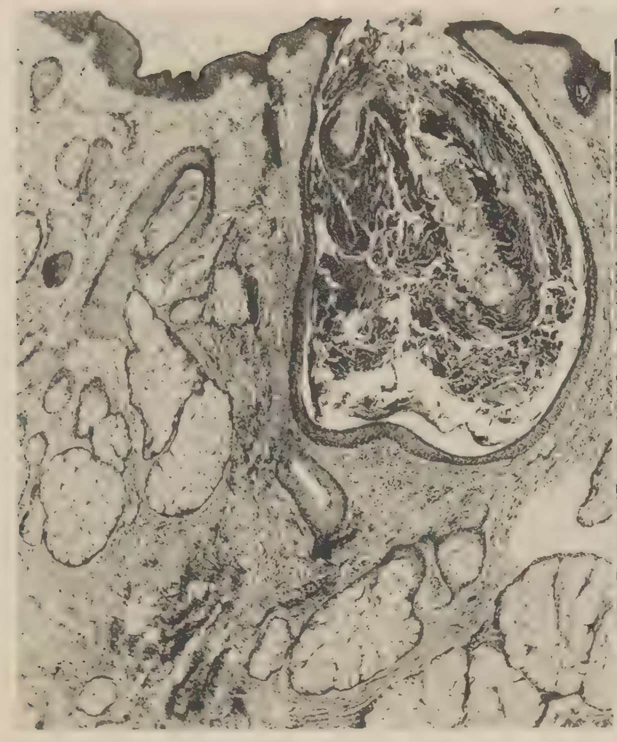


Section from trachea. Areas of vascularization with minimal exudate. Increase of chondrocytes in cartilage. x 120.

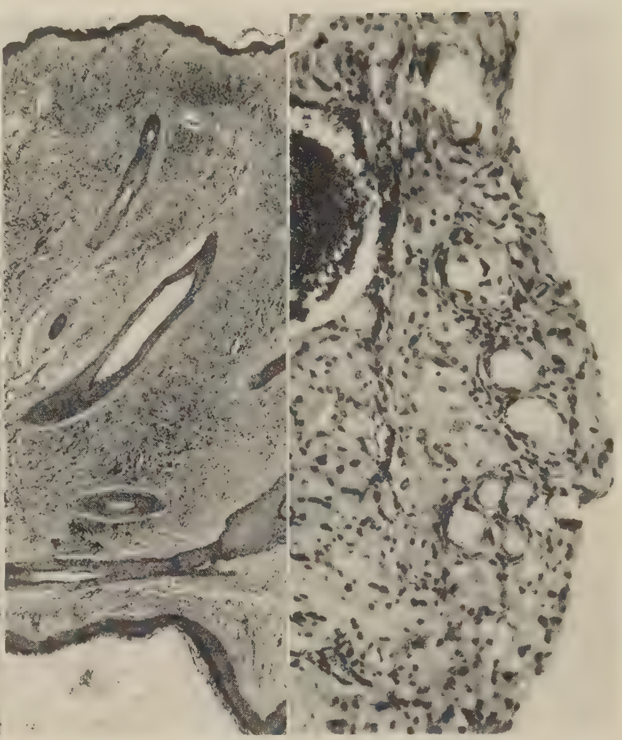


Another field from ear. Metaplastic bone and fibrous marrow replacing cartilage. x 150. (E. J. Gordon, Wash.)

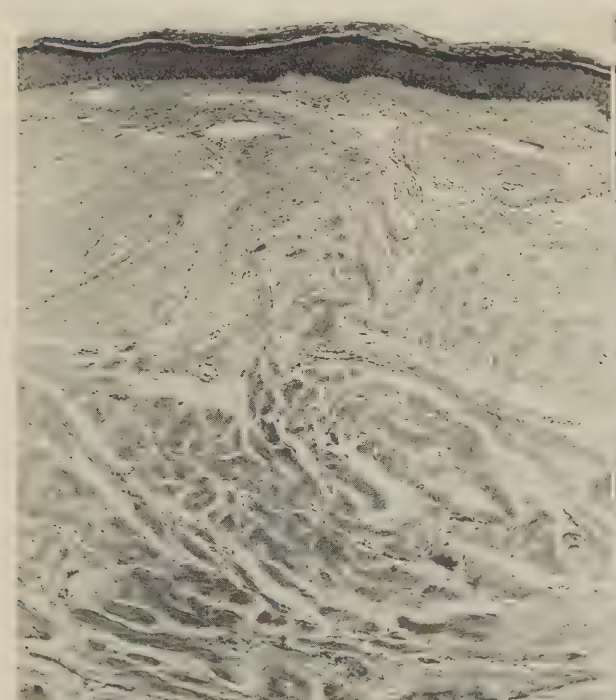
A remarkable case of unknown pathogenesis, in which cartilages of ear, larynx, nose and many joints were involved.



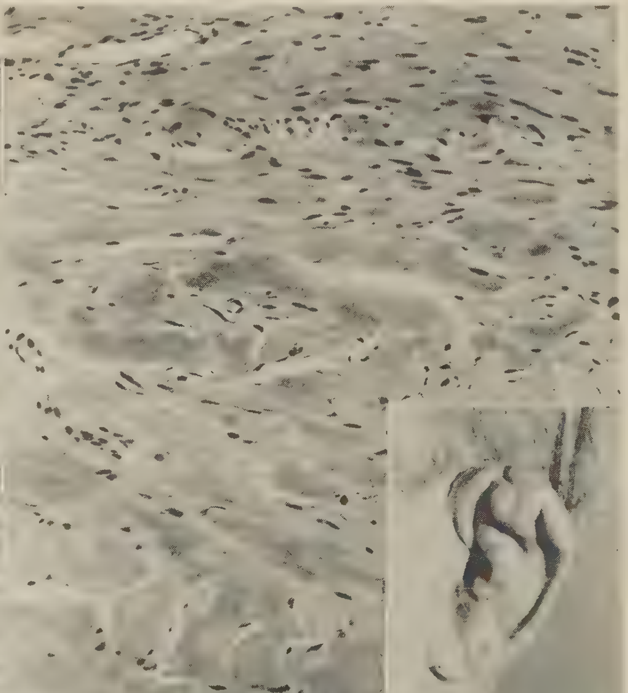
Comedo (black head), in a follicle, pinna. Orifice obstructed by dried keratin and sebum. The black color is due not only to dirt but to the chemically altered sebum. x 48.



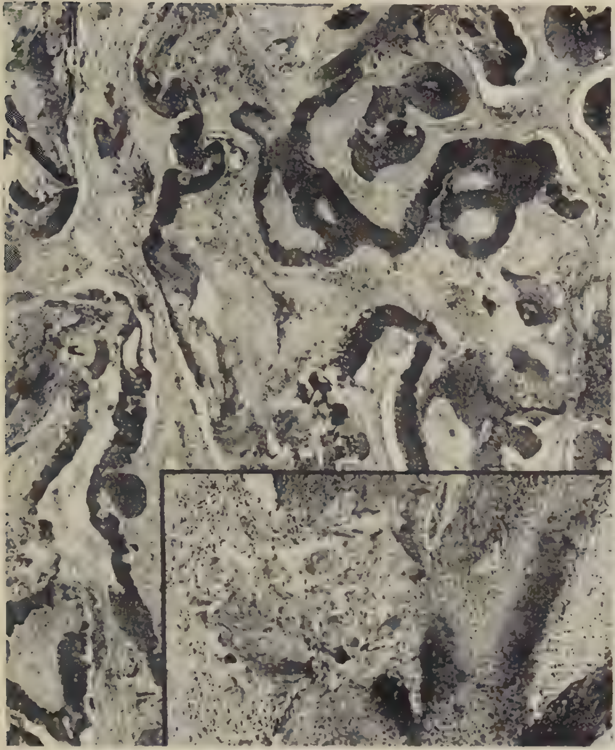
A. **Dermal nevus** and **sebaceous cyst,** ear. The nevus cells form a dark area in dermis, top; epidermis not involved. Segment of cyst wall, bottom. x 28. B. **Epidermal cyst.** Epithelium replaced by foreign body reaction, foam cells and giant cells. x 75.



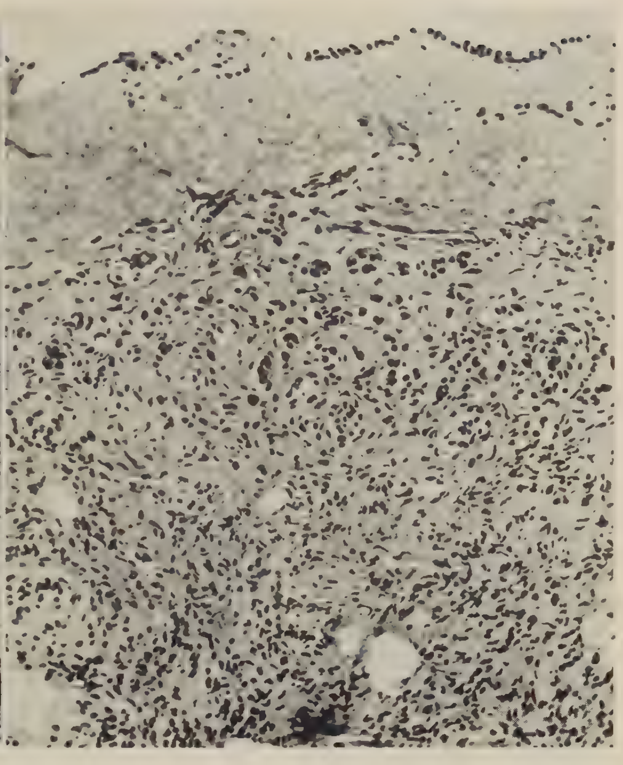
Keloid, a result of trauma:
Thick strands of acellular collagen have largely replaced collagen of the deeper dermis. x 48.



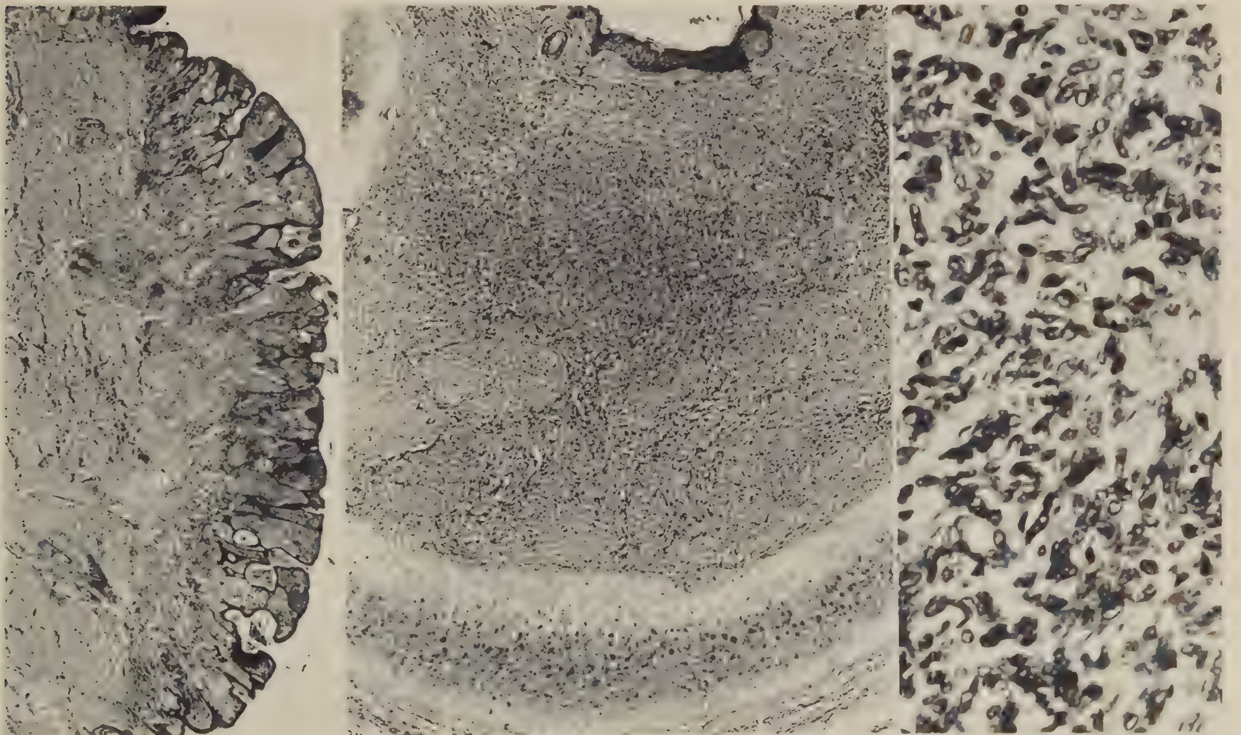
Cauliflower ear. The deformity is due to formation of keloid collagen, not to changes in the cartilage. x 125.



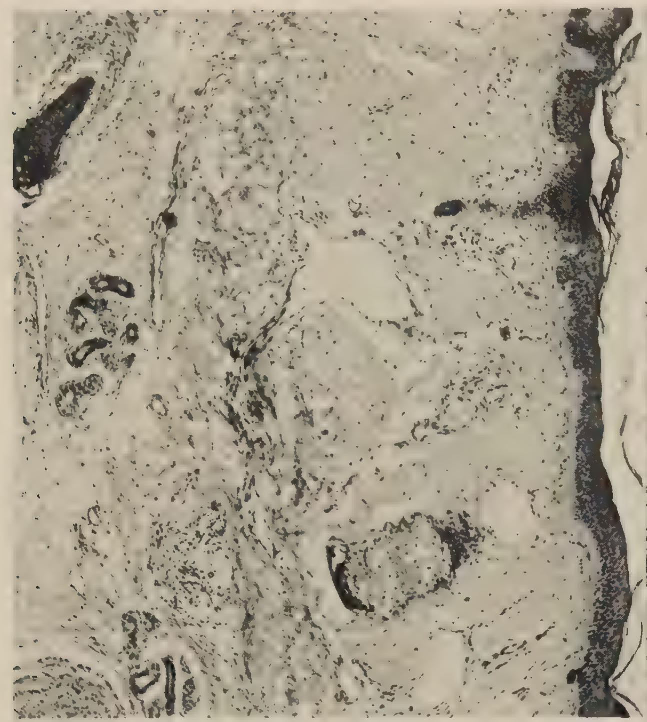
Calcifying epithelioma (epidermal inclusion cyst). Twisted strands of compact squamous epithelium and masses of keratin that may become calcified or ossified. x 12. Inset: foreign body reaction to keratin. x 21.



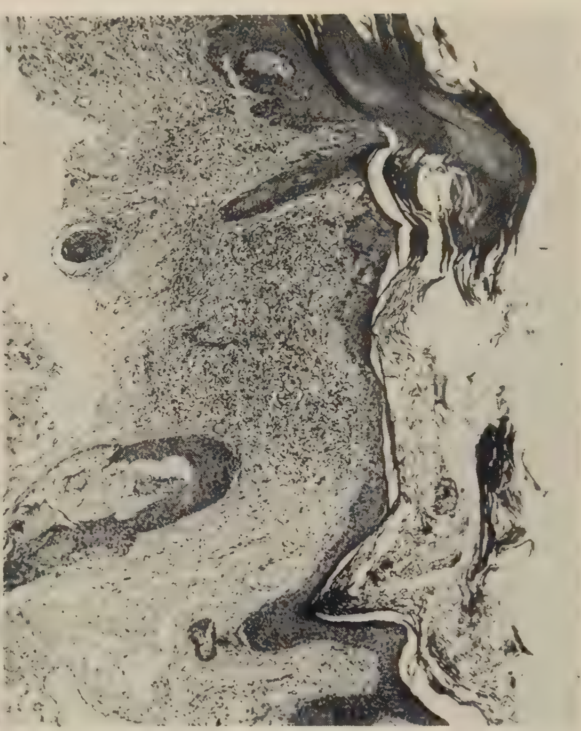
Neuronevus, concha; ulcerated for 15 years but still localized. Small groups of nevus cells under ulcerated, scarred surface of skin; palisaded nuclei of neural element deeper in section. x 125.



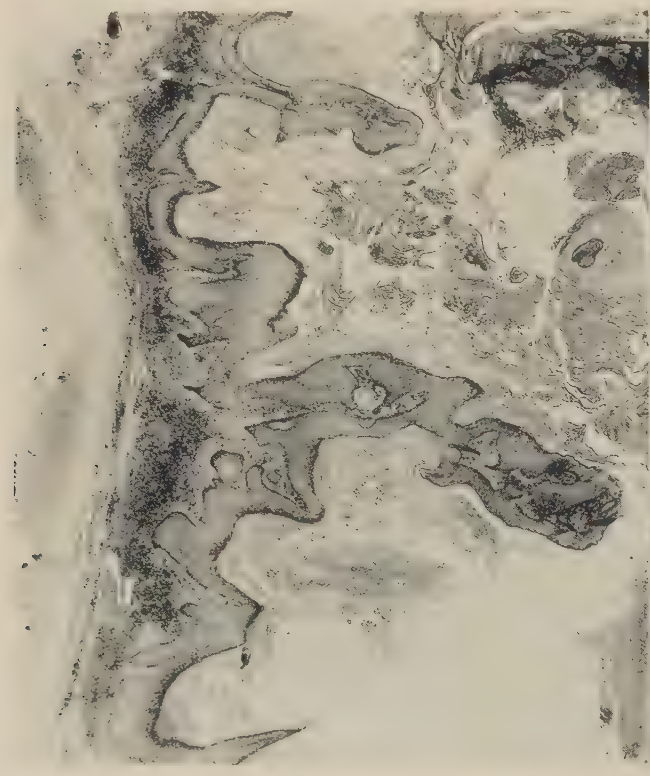
A. **Dermal nevus,** occupying large area on concha. Nevus cells sharply limited to upper dermis. B. **Dermatofibroma,** superior part of pinna, beneath helix, reaching cartilage. x 30. Unusual site. C. Characteristic pattern of stellate and spindle cells. Benign. x 45.



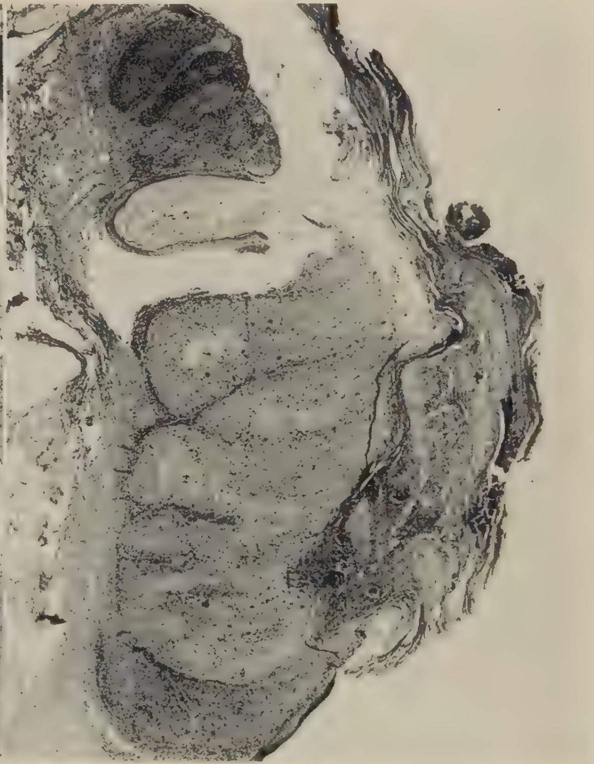
Atrophy of sweat glands and epidermis; collagenous degeneration of upper dermis; elastosis of deeper dermis (dark streaks down center) and dilated blood vessels are all senescent changes hastened by exposure. x 62.



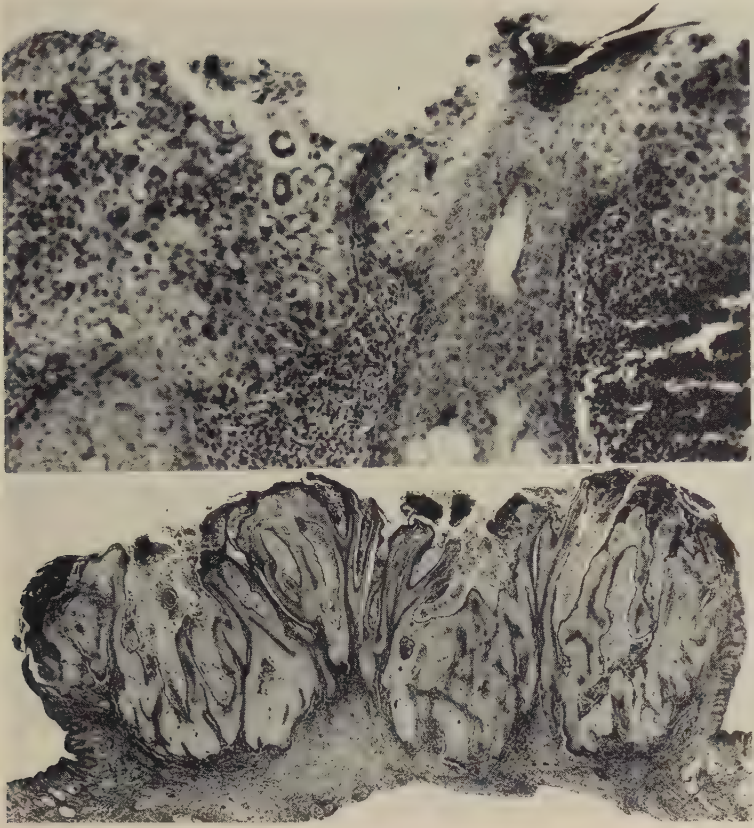
Senile keratosis, a more serious change in epidermis. In this section there is atrophy instead of the usual acanthosis. Excess keratin; elastosis of dermis. x 48.



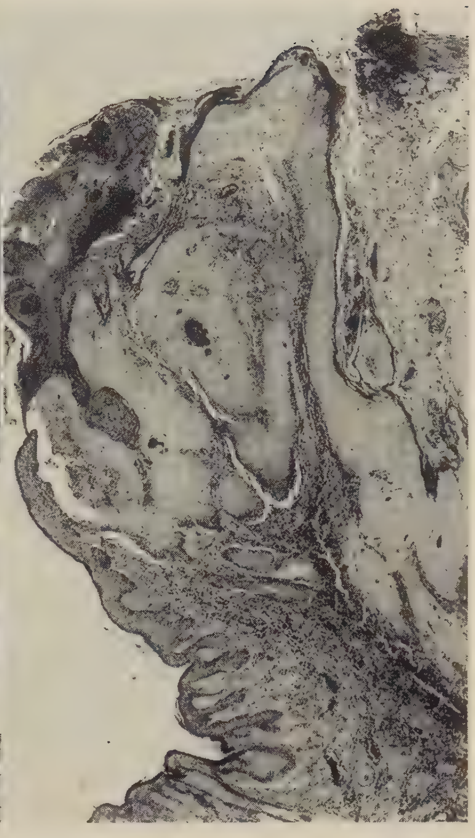
Senile keratosis, verrucous type; a precancerous lesion. x 16.



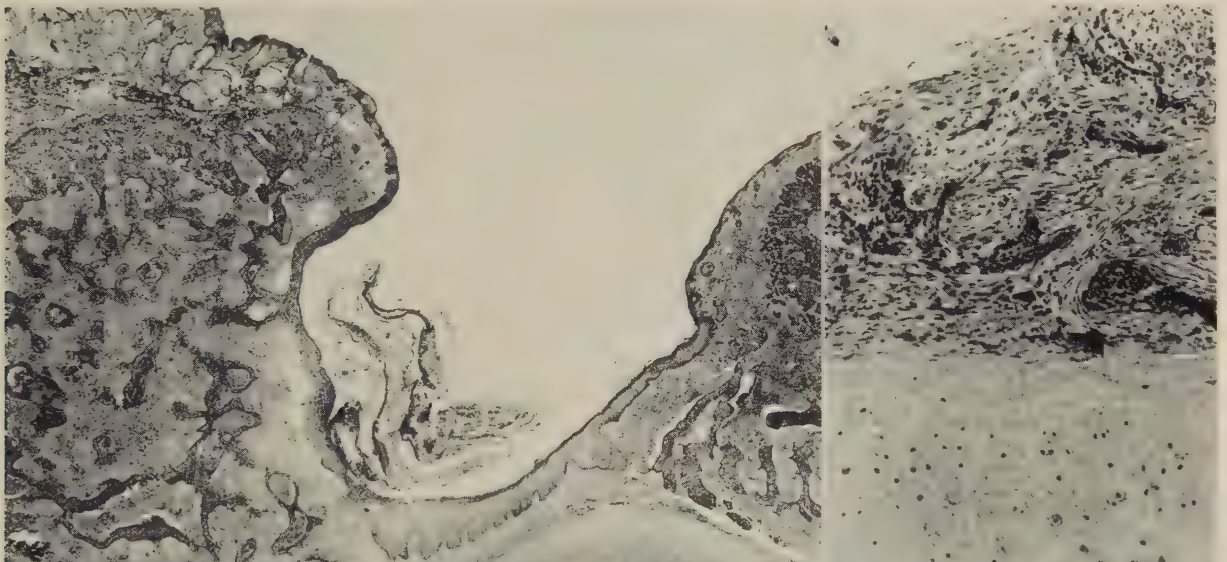
Senile keratosis with localized acanthosis and hyperkeratosis. Malignant dyskeratosis of the deeper epithelium; early squamous cell carcinoma. x 21.



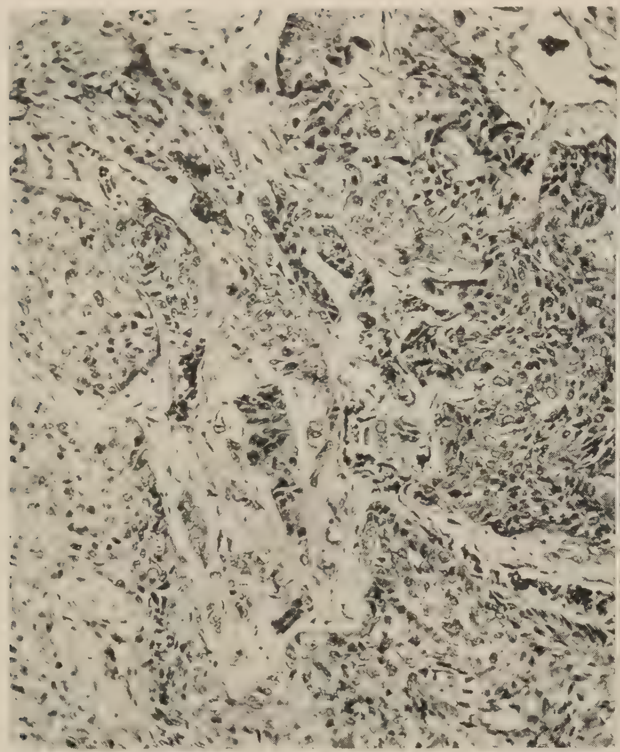
Senile keratosis, with dyskeratosis of the Bowen type; scattered bizarre cells in prickle layer *(upper)*. This is not clinical Bowen's disease. Invasion has not yet occurred. x 125. Senile keratosis of a warty, papillary type *(lower)*. Not frankly malignant at this time. x 7.



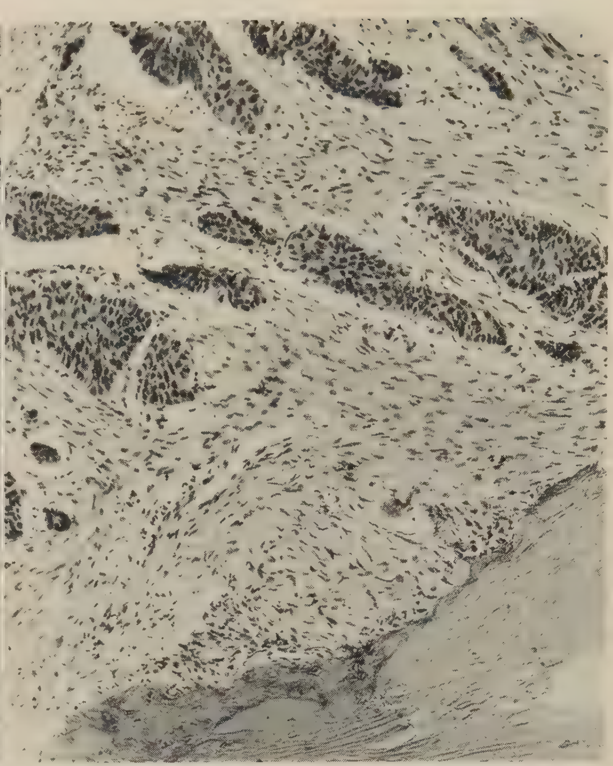
Dyskeratosis is evident in the acanthotic pegs; basal layer is still well defined. x 24.



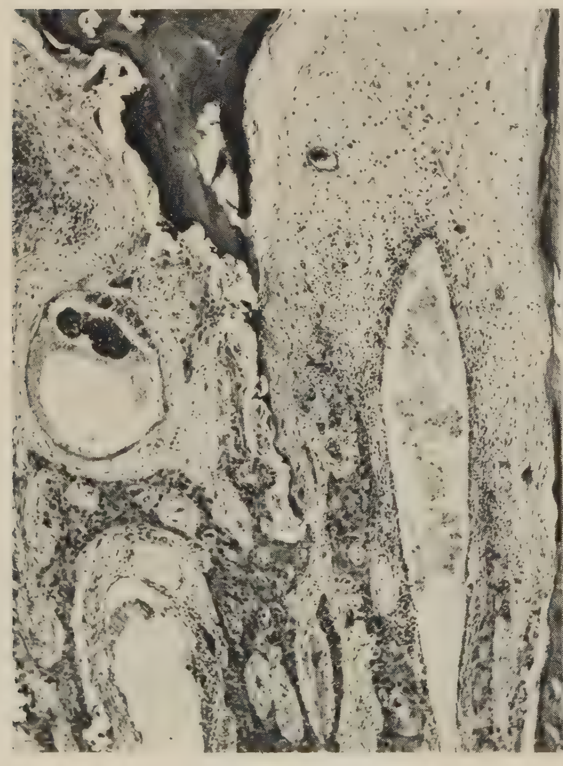
Basal cell carcinoma of long standing, upper edge of ear. Central portion of dermis still close to cartilage, but around this hyperkeratotic crater the epidermis is elevated by invading tumor. x 12. Nests of basal cells have reached the cartilage. x 91.



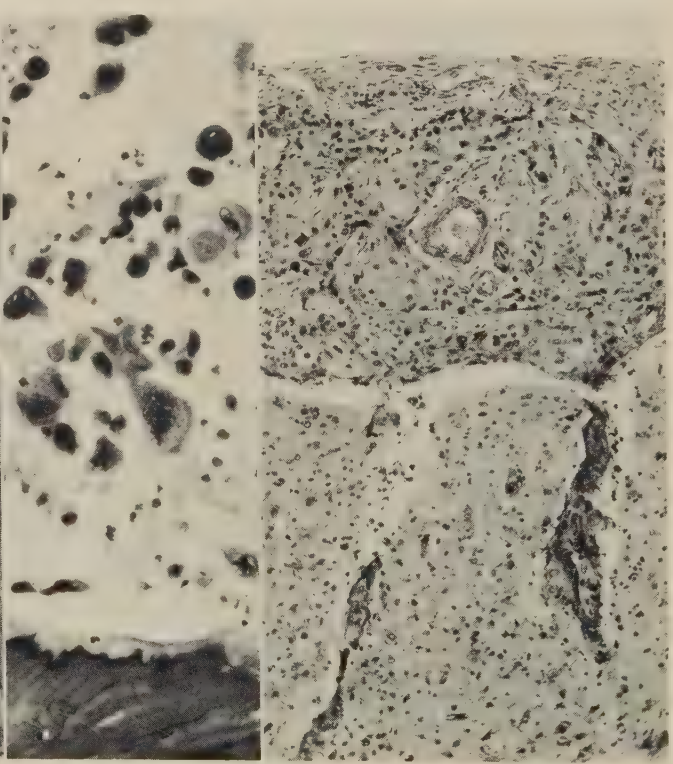
Squamous cell carcinoma, fairly well differentiated, arising in post auricular skin and extending into mastoid. x 125.



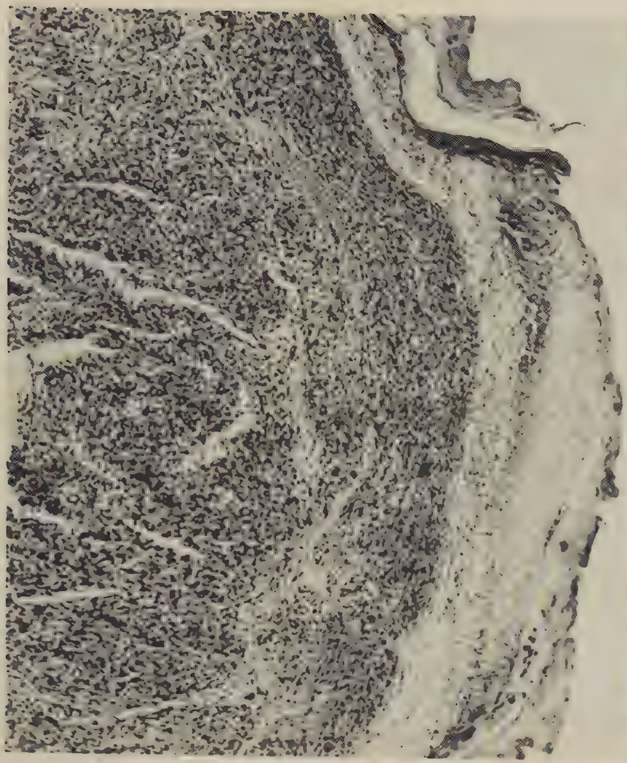
Squamous cell carcinoma, not well differentiated in this field but showing pearls elsewhere, primarily in preauricular skin and invading mastoid. Bone at bottom. x 90.



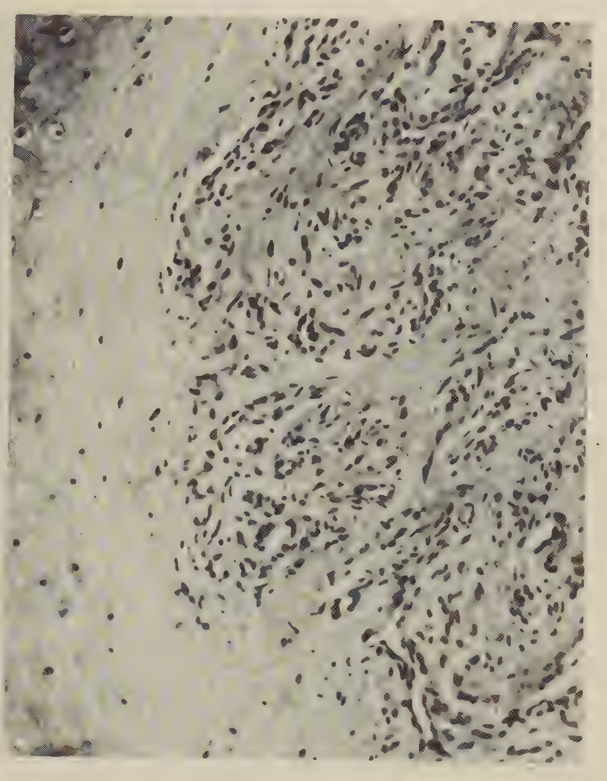
Squamous cell carcinoma, external ear, although well differentiated, has invaded petrous bone. x 48.



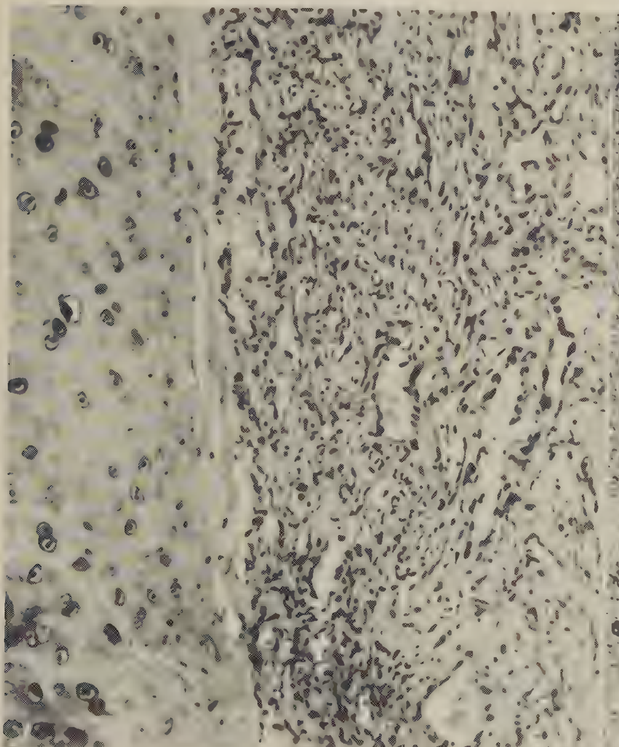
A group of bizarre cells from same tumor (left). x 275. The tumor invaded through the meninges into the brain (right). x 160.



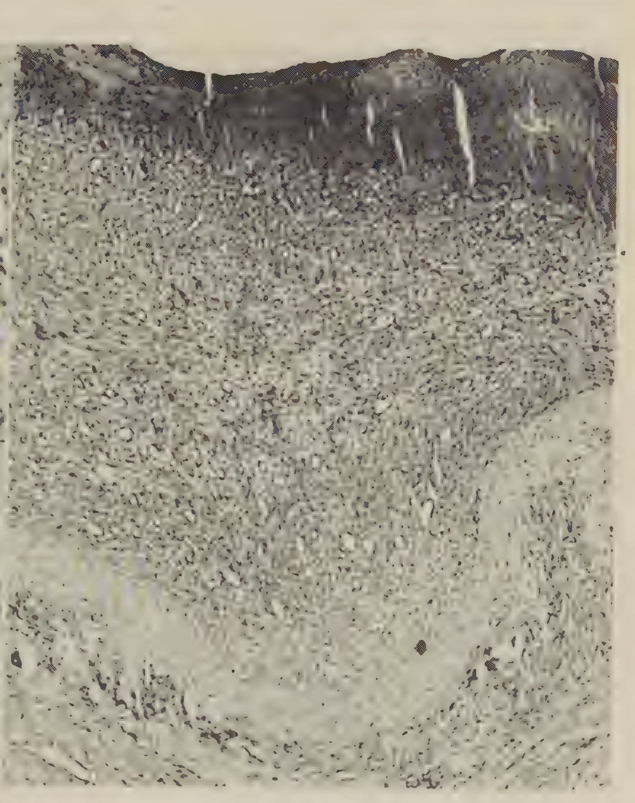
Atypical granuloma pyogenicum, diagnosed angioendothelioma. More than usual number of cells between vessels; surface necrotic. x 70.



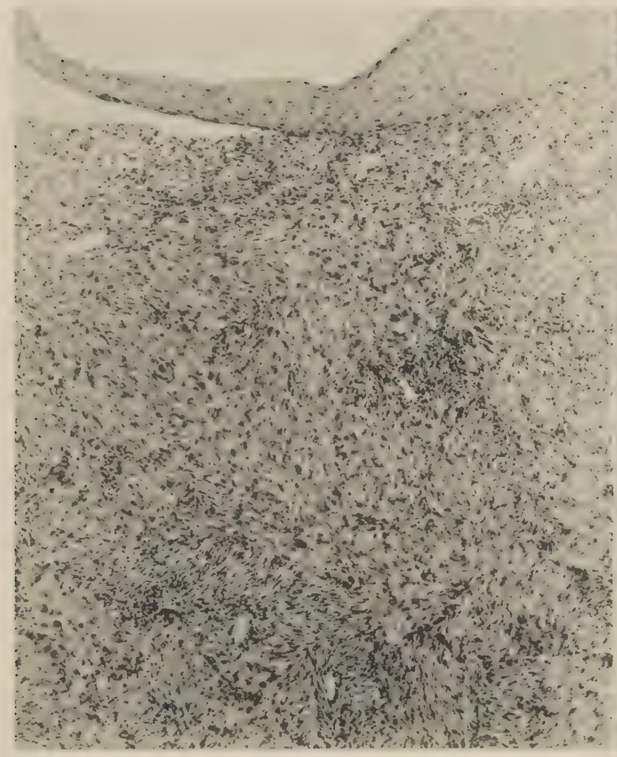
Infiltrating capillary hemangioma, invading cartilage of ear. x 120.



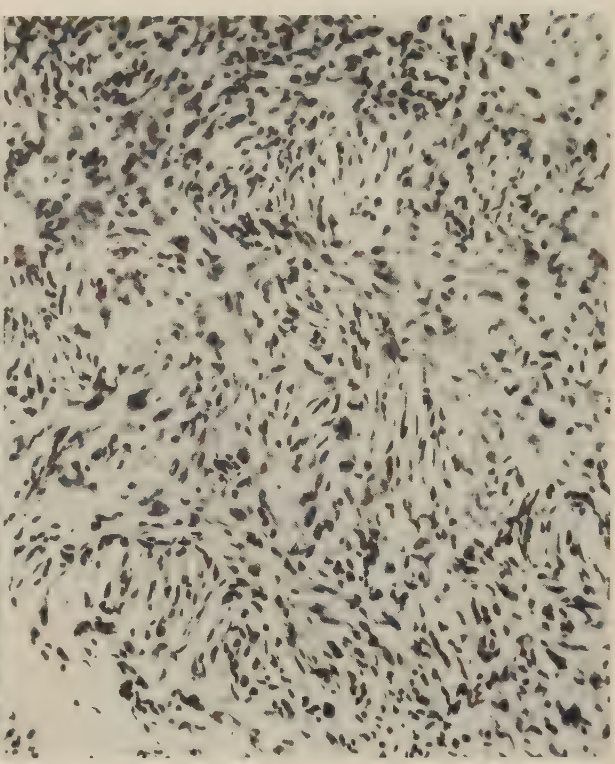
Congenital hemangioma, ear, that was severely traumatized. It has reached the cartilage. x 125.



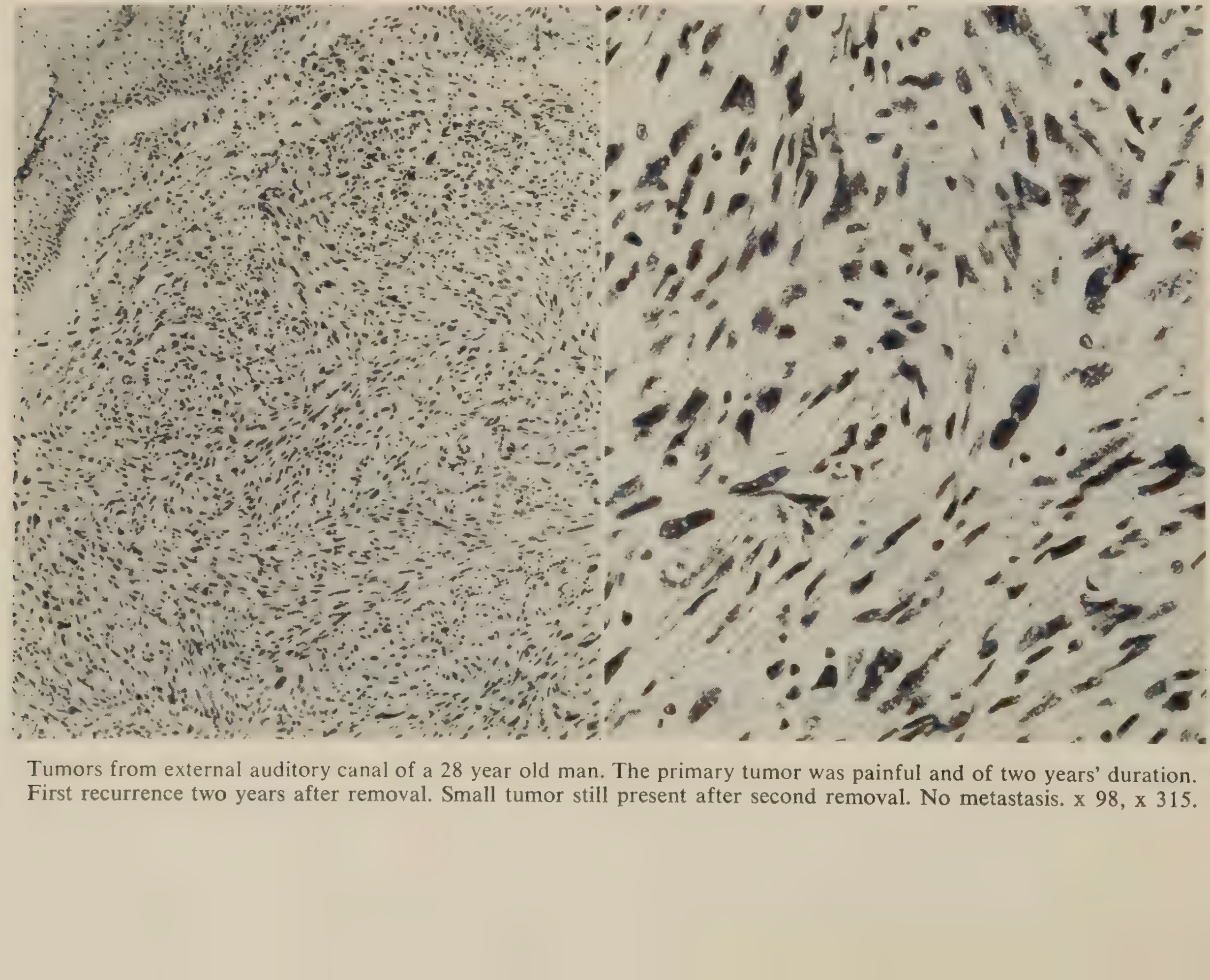
Organizing blood clot in subcutaneous tissue of ear, simulating capillary hemangioma. x 62.



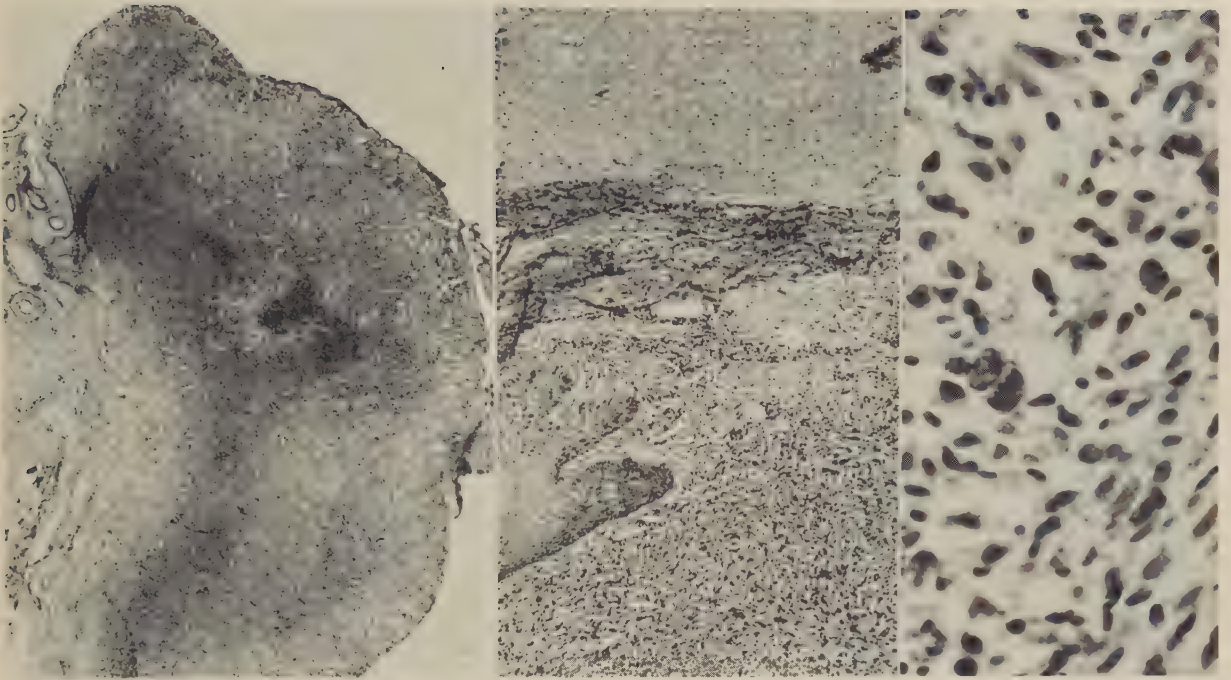
Dermatofibroma protuberans:
Cell pattern is more neoplastic than those of related benign dermatofibroma and sclerosing hemangioma. Recurrence is frequent and metastasis possible.



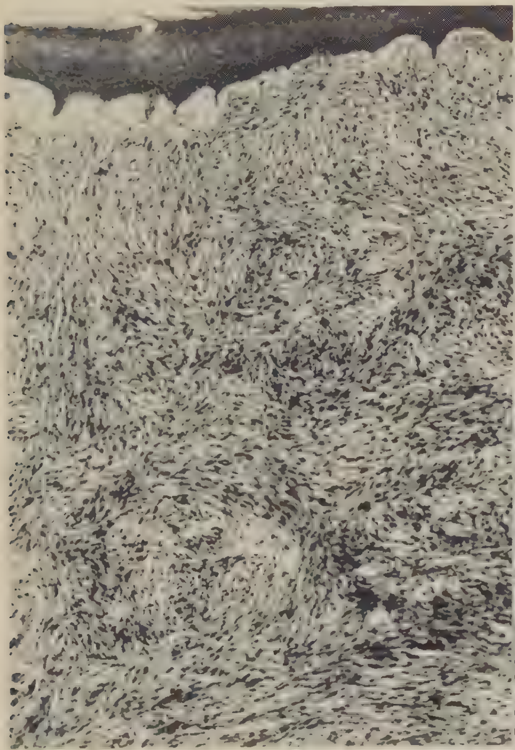
Recurrent tumor, diagnosed neurofibroma because of apparent palisading of nuclei. Note bizarre stellate nuclei. x 160.



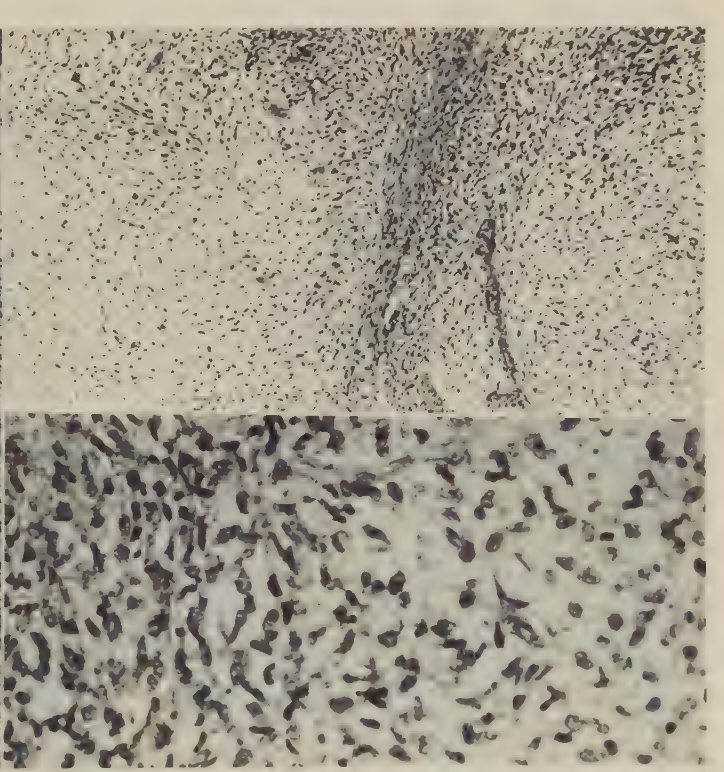
Tumors from external auditory canal of a 28 year old man. The primary tumor was painful and of two years' duration. First recurrence two years after removal. Small tumor still present after second removal. No metastasis. x 98, x 315.



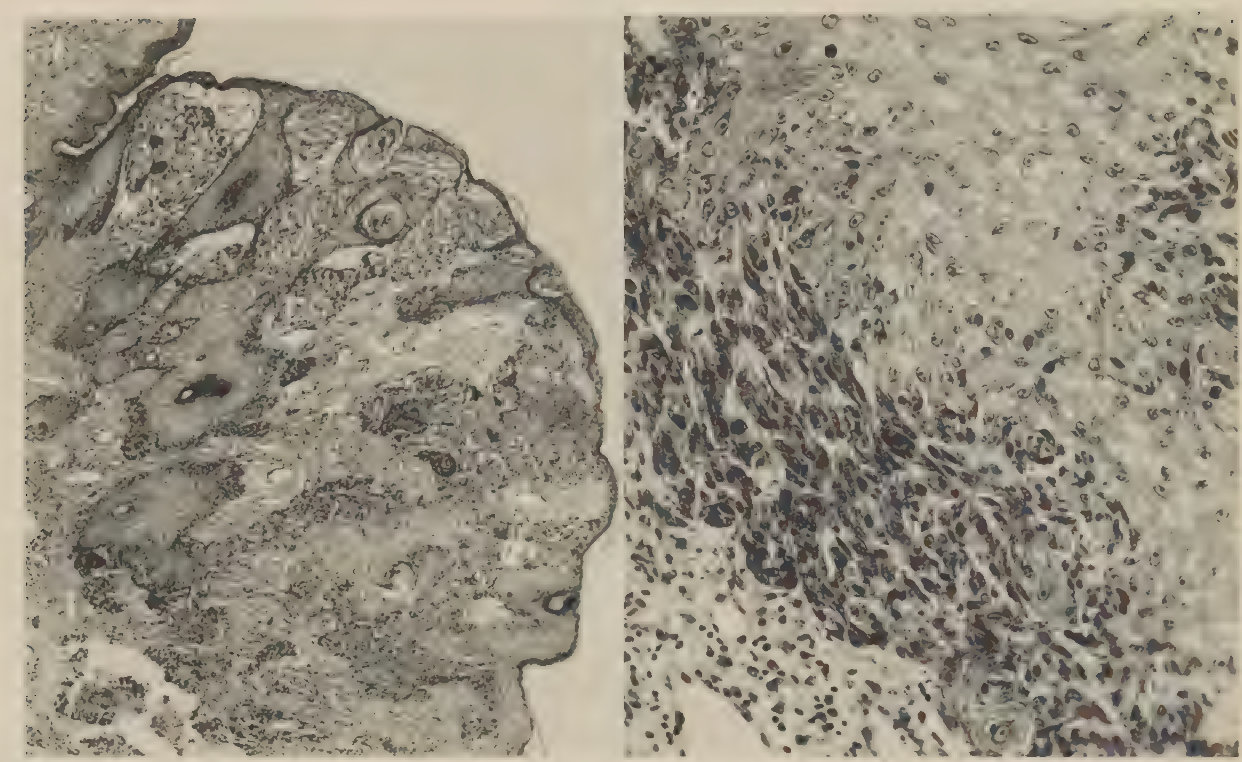
Fibrosarcoma. Firm, poorly circumscribed mass in dermis of external ear. Atrophy and focal erosion of surface epithelium. x16. Cellular, well vascularized tumor composed of spindel cells with fibrous processes has infiltrated to perichondrium. x70. Variation in size of cells; hyperchromatic occasionally atypical nuclei; frequent mitoses. x450.



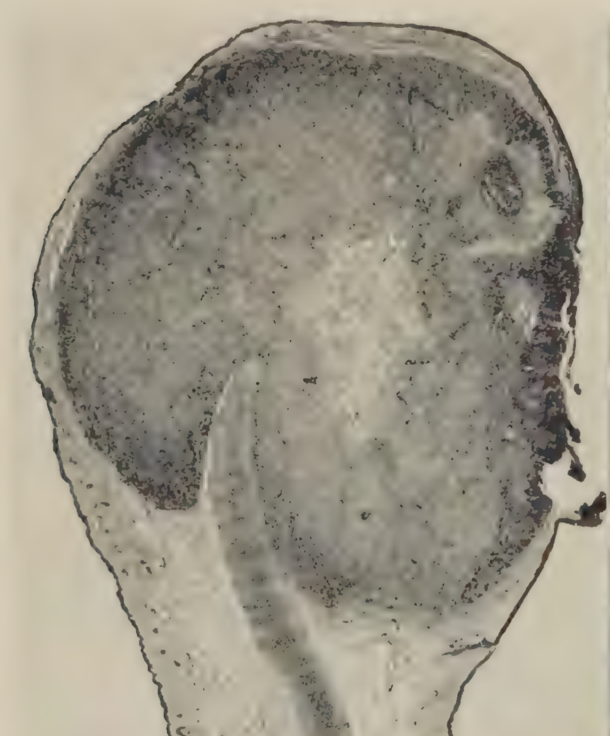
Fibrosarcoma with long spindle cells and prominently interlacing fascicles producing whorled pattern, superficially resembles leiomyosarcoma. Mass on helix, 2 cm. in diameter, from a 60 year old man.



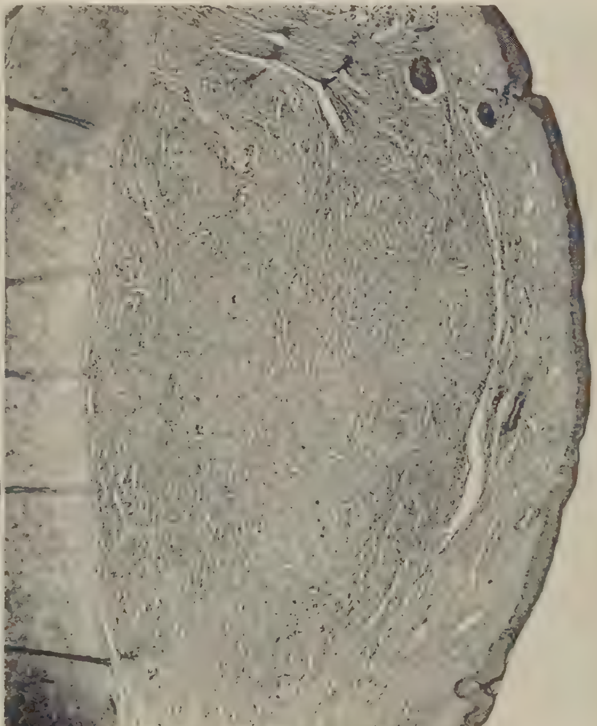
Myxofibrosarcoma, possibly embryonal rhabdomyosarcoma, lacking well differentiated foci. Polypoid mass in 5 year old boy promptly recurred; death five months later, with extension locally and into neck, but no metastases. Spindle and stellate cells with delicate processes. x62, x457.



Dermal-epidermal nevus (junctional), skin of ear. Small lesion showing massed nevus cells in dermis, clear cells and small groups of nevus cells in basal layer of epidermis. Many of the cells are spindle type and contain much melanin. Potentially malignant. x 39, x 210.

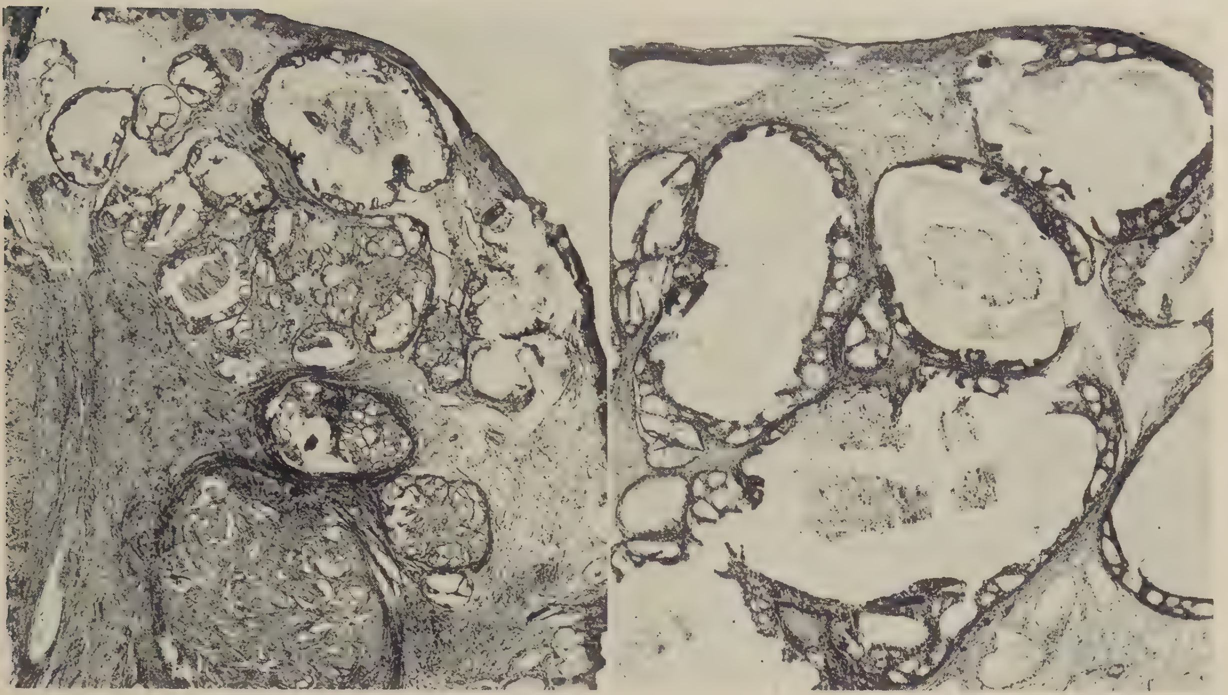


Malignant melanoma developing in a local nevus on helix. Solid mass of epithelioid cells. x 8. Subsequent history not known.

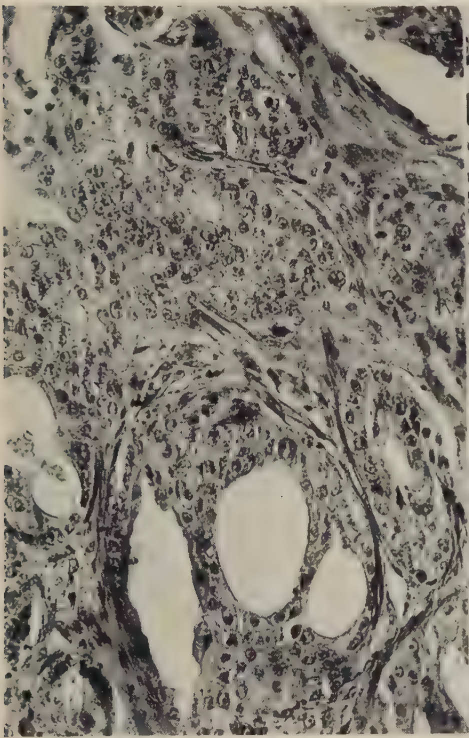


Malignant melanoma, amelanotic, recurring after two previous biopsies diagnosed respectively basal and squamous cell carcinoma. x 28.

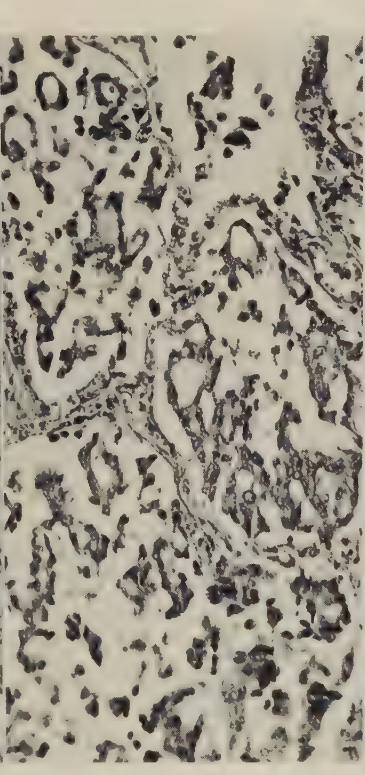
ADNEXAL CARCINOMA



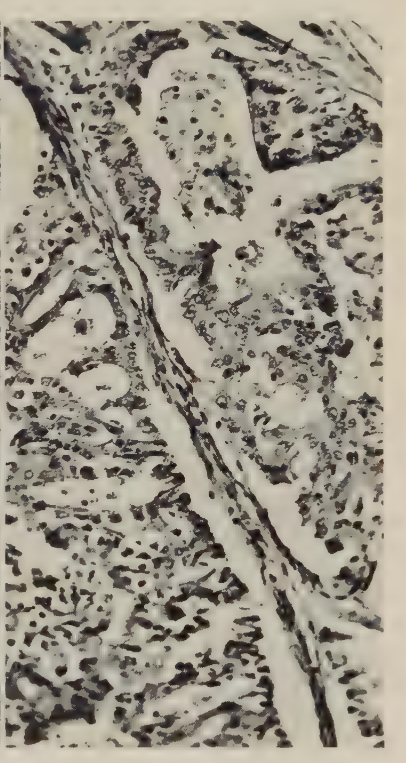
Adnexal carcinoma of probable sweat gland origin, skin of right ear and external auditory canal, from a 55 year old man with right facial paralysis for two years and increasing deafness. First noted four years previous as small lesion that changed very little. Surface of excised tumor has cystic and glandular structure considered compatible with ceruminous or sweat gland origin. x16, x48. Death a year later with metastases to lungs, dura, retroperitoneum and bones.



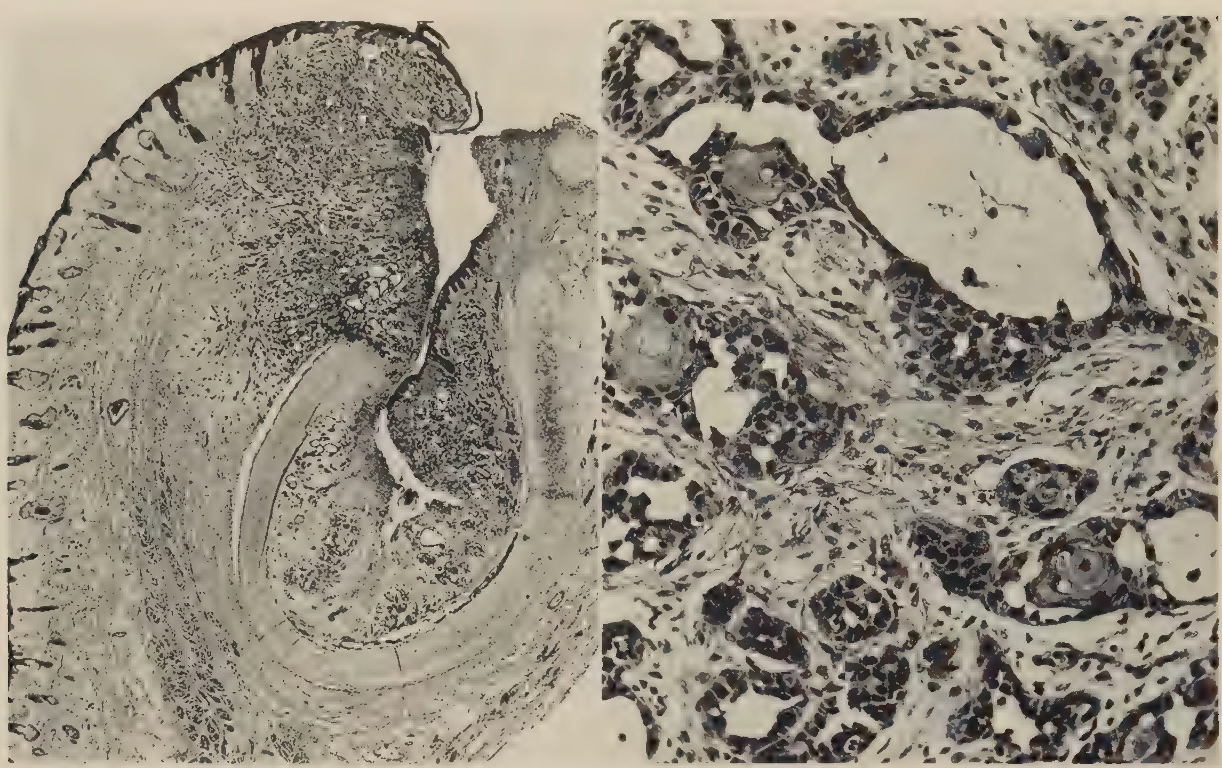
Deeper infiltrating areas have more solid structure, fairly uniform cells, frequent mitoses. x185.



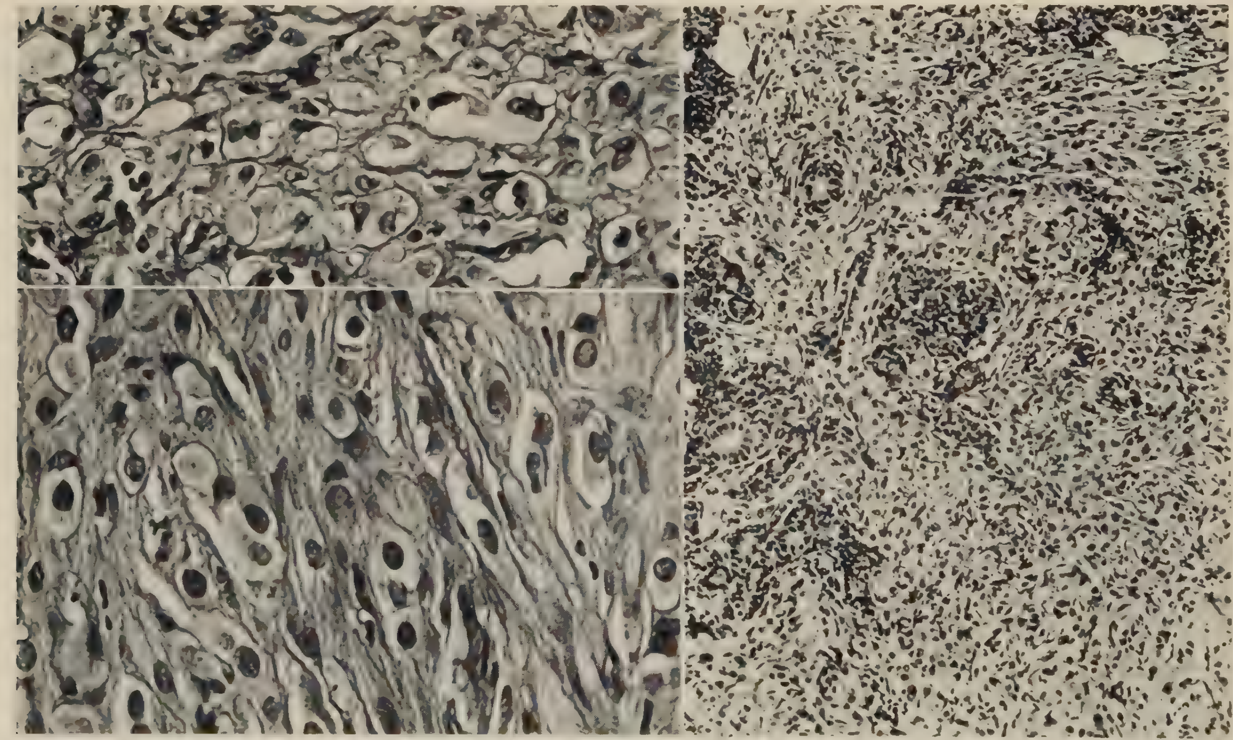
Lung metastasis retains adenocarcinomatous structure of primary tumor. x145.



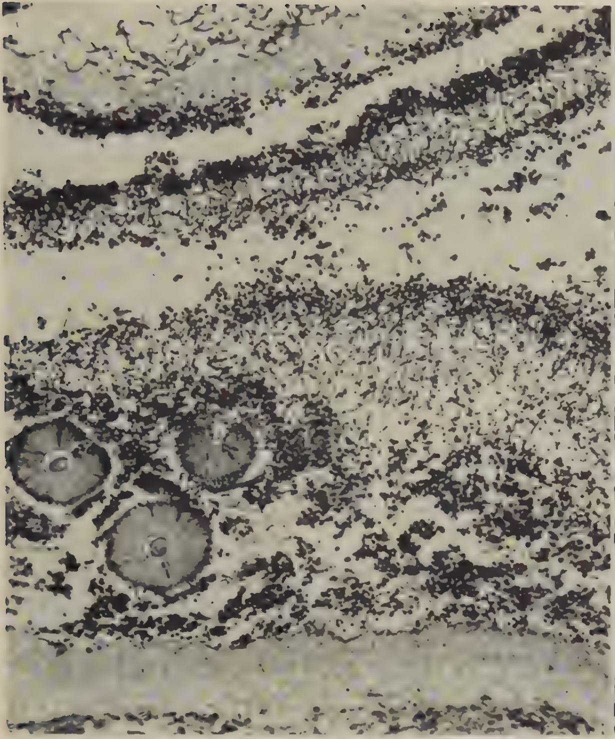
Metastasis to dura over right temporal bone has well differentiated glandular pattern. x125.



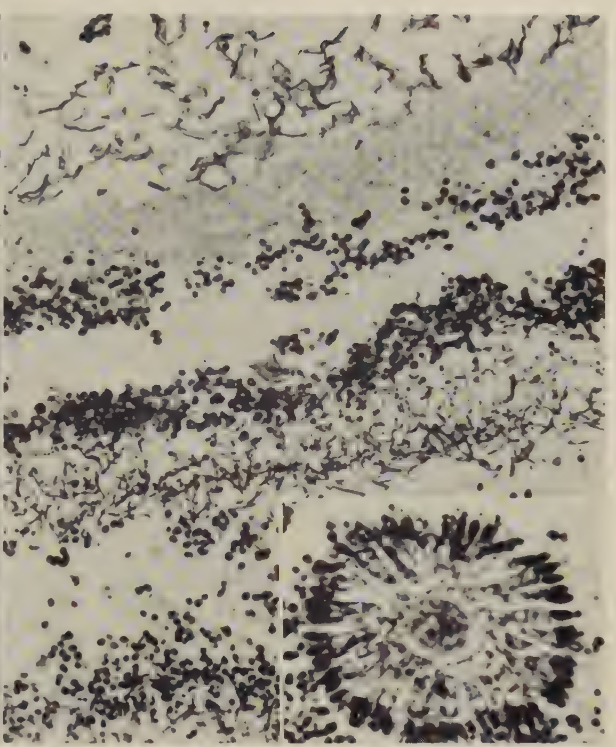
Carcinoma, possibly from sweat gland, invading down to cartilage, from a 57 year old man. Despite repeated surgery and irradiation therapy, it invaded mastoid in course of three years. Adenomatous and cystic pattern resembling that of tumor on previous plate, but, in addition, a definite squamous tendency. x 8, x 125.



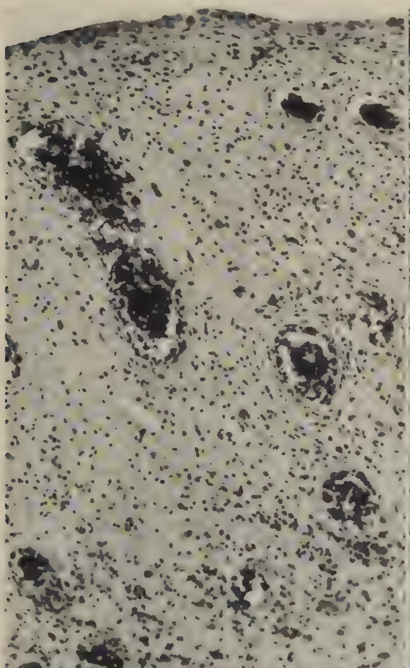
Undifferentiated tumor. Ulcerated lesion present for nine months on back of helix of 7 year old white girl. Diagnoses included sweat gland tumor, neurofibroma and myoblastoma. Cervical nodes enlarged. Involved portion of ear, parotid, and nodes removed February 1951. No recurrence, June 1951. A. Tumor in ear. x 395. B. As it invaded the parotid. x 475. C. Lower magnification of parotid tumor. x 114. (I. M. Wise, Mobile, Ala.)



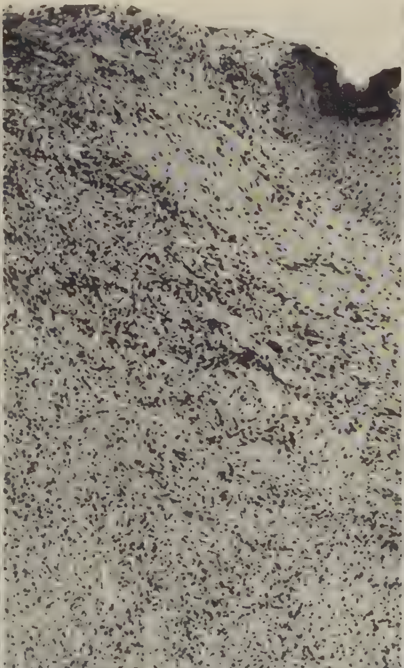
Otomycosis *(Aspergillus),* external canal: "False membrane" removed from external canal of 28 year old woman with tuberculosis and otitis of both canals. Compact keratin with masses of mycelia between. Very little exudate. x 90.



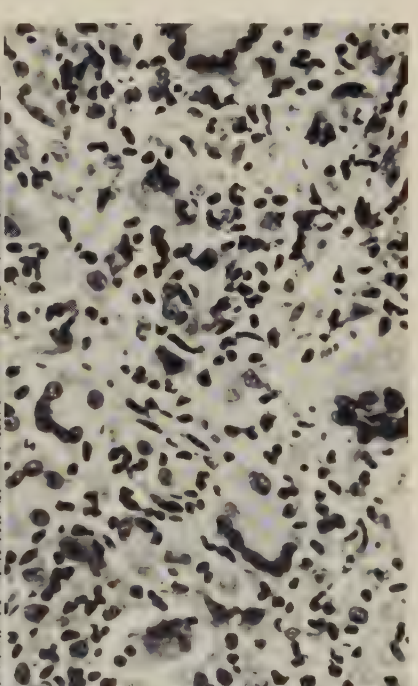
Keratin flakes, at top, mycelia and conidia (black dots) form bulk of membrane. x 165. Inset: A characteristic ray colony of mycelia. x 435.



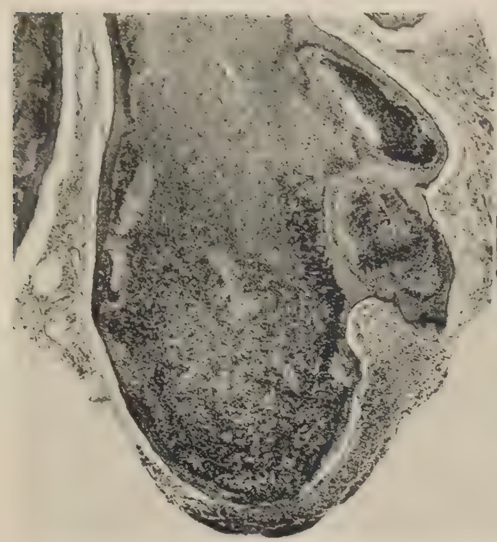
Mass of fibrosing granulation tissue from canal, clinically regarded as a tumor. x 125.



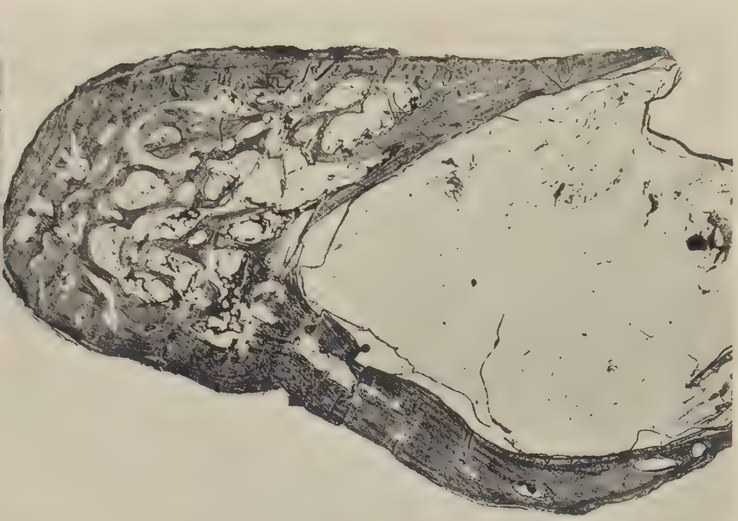
Granuloma pyogenicum from canal. Mass of blood vessels; ulcerated surface; purulent exudate. x 91.



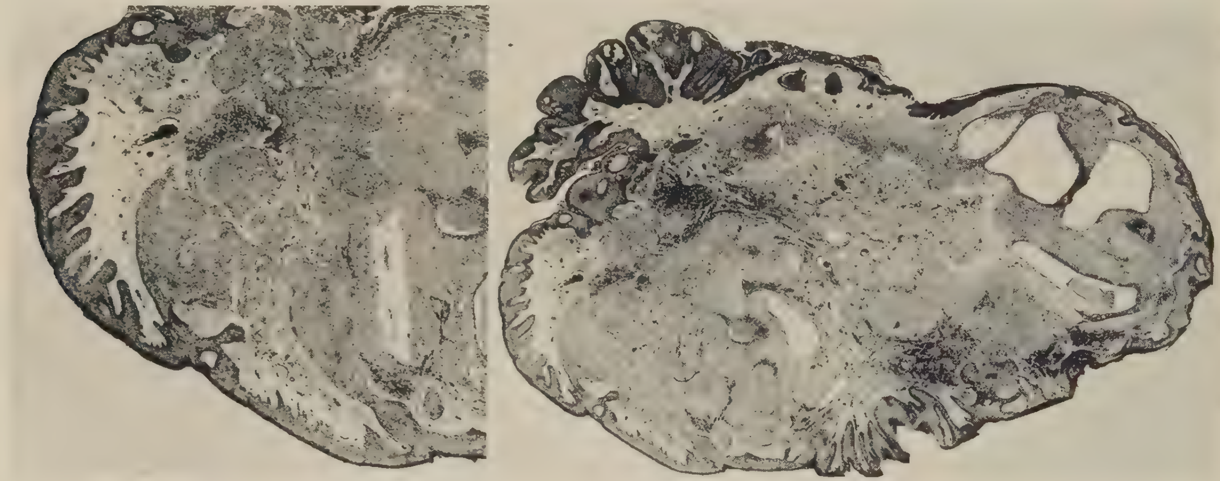
Xanthoma in canal. Foamy histiocytes and Touton giant cells. Benign. x 275.



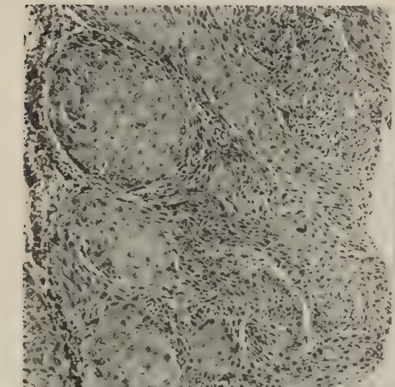
Intradermal nevus. Papillary, very cellular and heavily pigmented lesion in canal. Excess surface keratin. Benign. x 27.



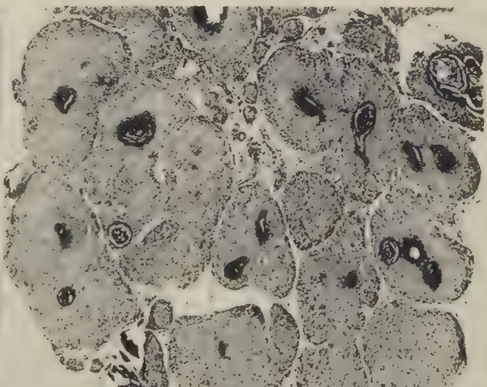
Sebaceous cyst. Tumor near external orifice of canal, movable but of bony consistency. Epidermal lined cyst in a capsule of metaplastic bone. x 11.



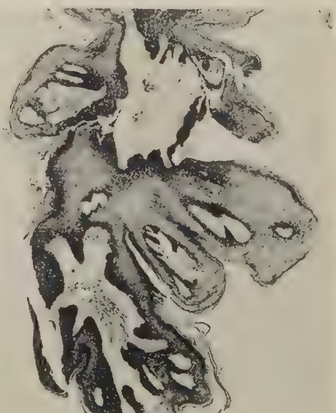
Adnexal adenoma, probably of sweat gland. Cysts enclosed in thick layers of benign epithelium. x 9, x 16.



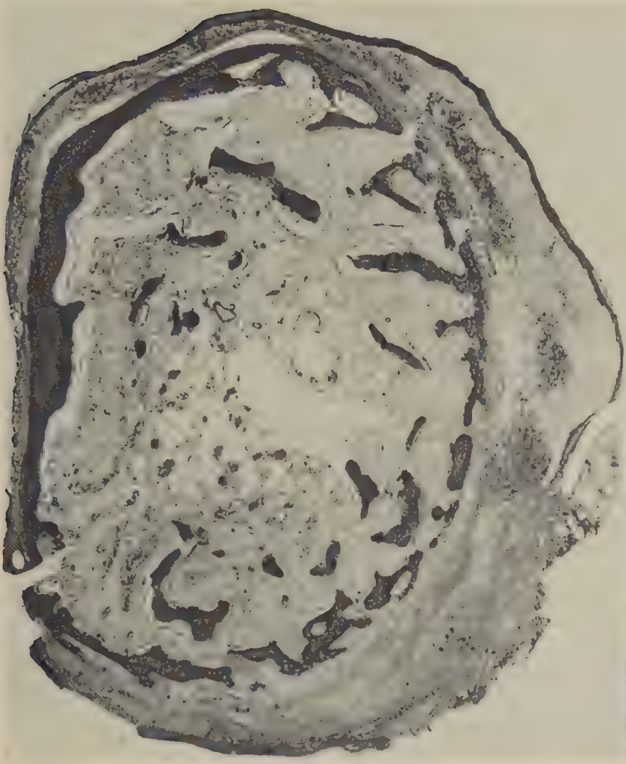
Epithelium is definitely dyskeratotic, suggesting potential malignancy. x 62.



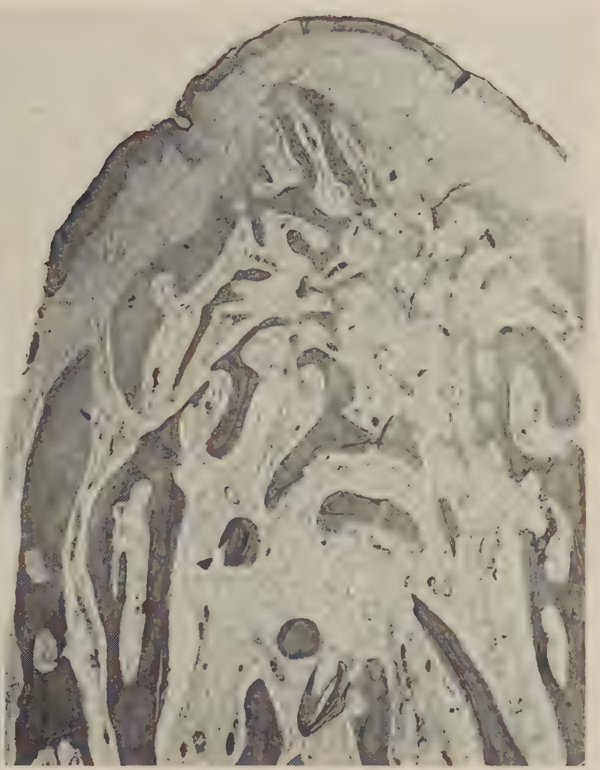
Clinically soft tumor; thick epithelium with delicate fibrous stalks. x 33.



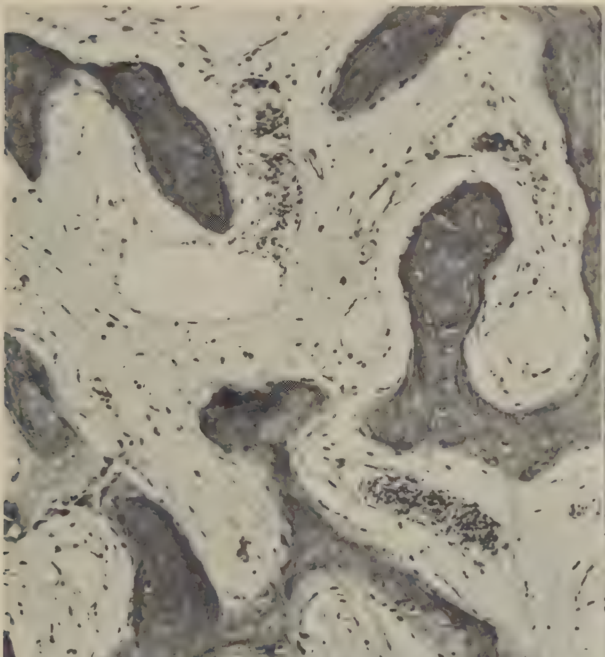
Squamous cell papilloma: Well differentiated epithelium; sharply defined basal layer.



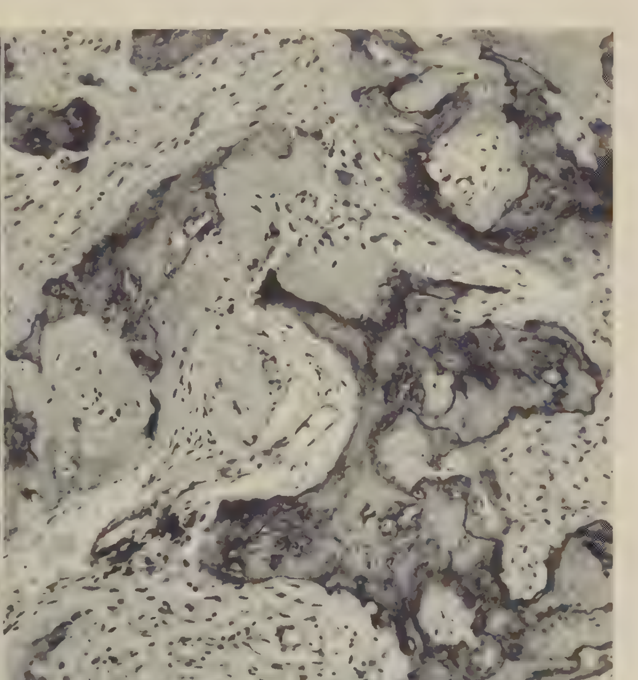
Osteoma, at junction of osseous and cartilaginous portions of canal, in an 18 year old girl. Thin shell of cortical bone and very trabecular, chiefly fibrous center. x 28.



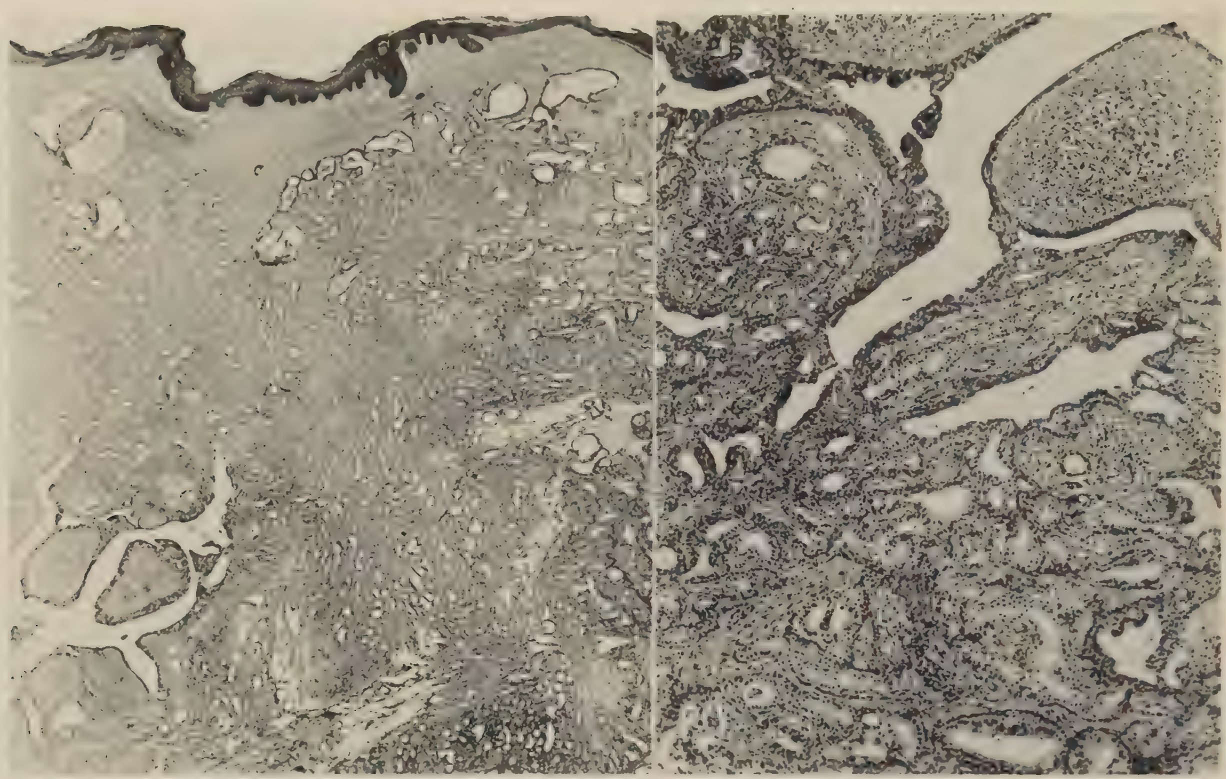
Osteoma, showing better organized bone. Squamous mucosa intact. x 27. Some prefer to call these lesions exostoses.



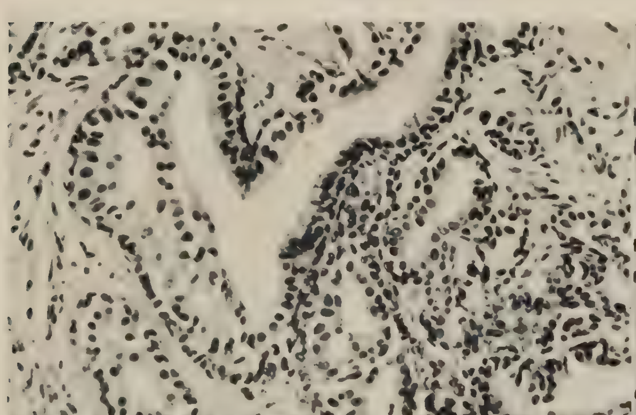
Osteoma. Of osteoid bone, the trabeculae are built up by a layer of osteoblasts. No fatty marrow, but vascular fibrous tissue obviously osteogenic. x 160.



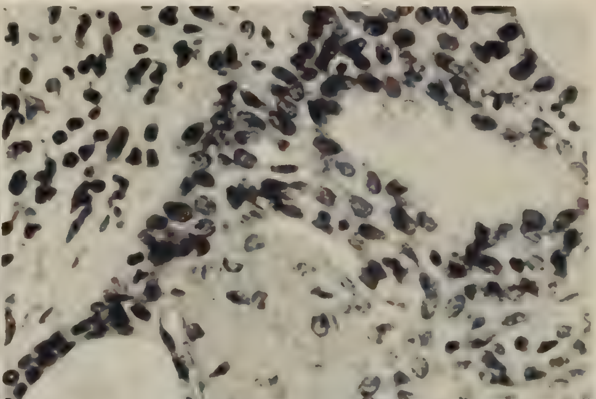
Paget's disease, involving entire temporal bone. This specimen from external canal. The irregular mosaic pattern of the trabeculae is characteristic. x 125.



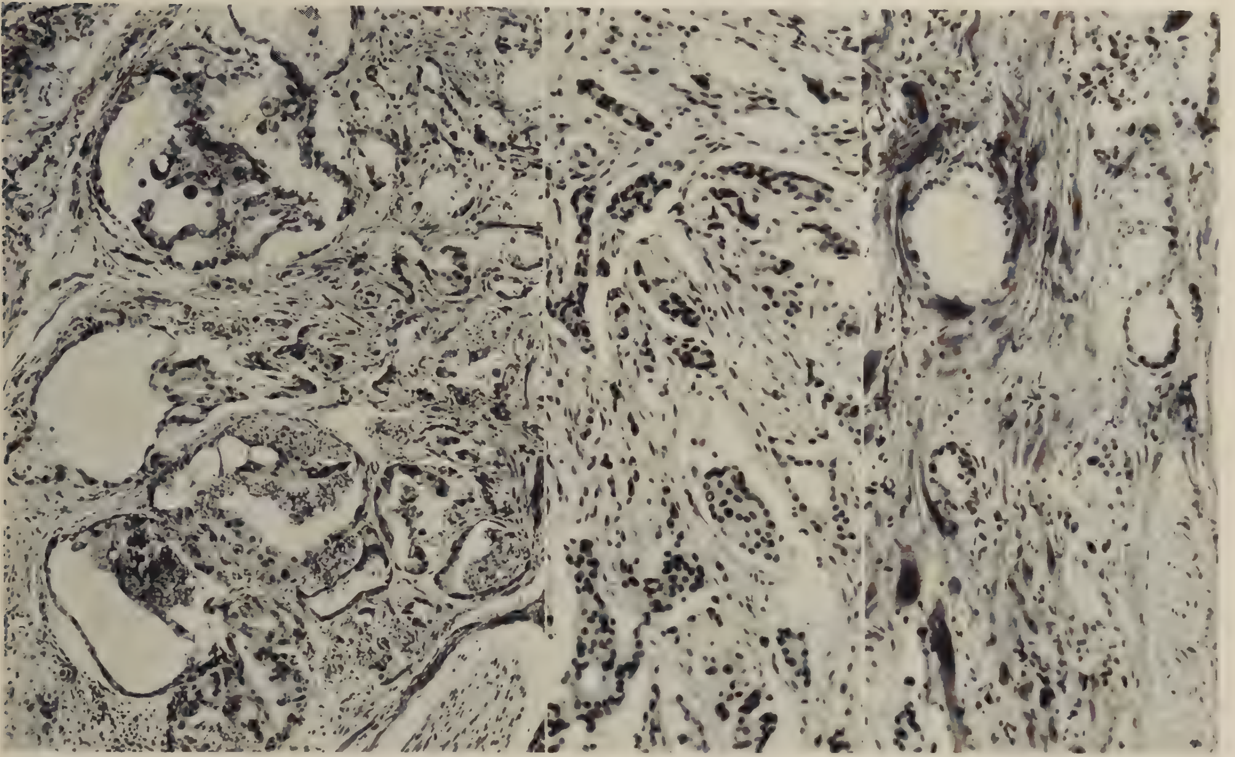
Adenoma of ceruminal glands, external auditory canal, of four years' duration, in a 45 year old woman. Removed en masse by blunt dissection from bony canal. It was diagnosed carcinoma, but there has been no recurrence in 12 years. Glands of irregular shapes and sizes. x 20, x 62. (S. S. Hall, Clarksburg, W. Va.)



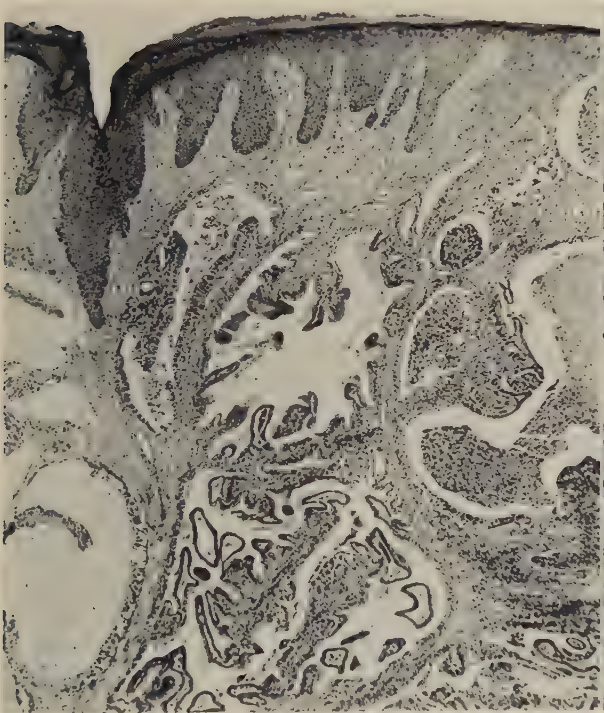
Epithelium is generally columnar and forming glands, but there is considerable variation in cell type and arrangement. x 165.



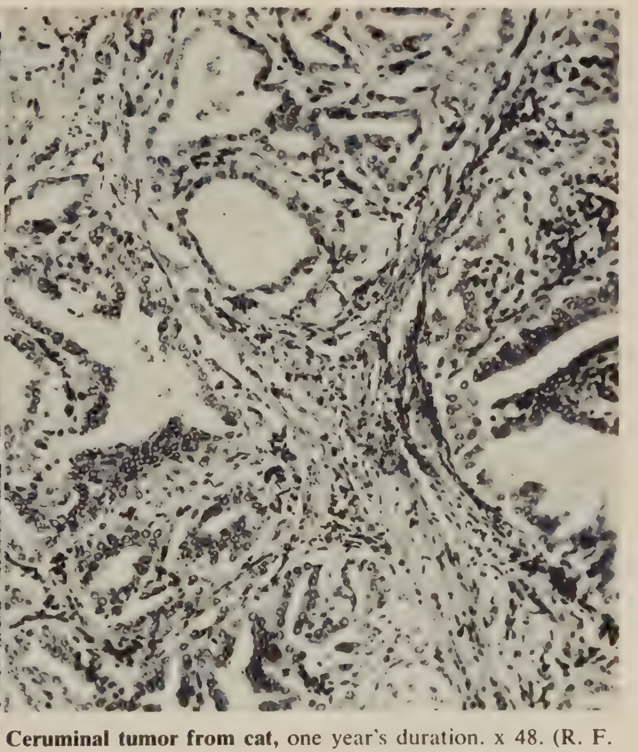
The structure of gland (at top), apocrine-type epithelium discharging small globules, is normal for ceruminal glands. Area of squamatoid cells in center. x 400.



Adenoma, ceruminal glands, from man. Originally diagnosed adenocarcinoma. There is much greater variation in cell type and pattern than in the adenoma illustrated on the previous plate. Many areas look like aggressive malignant infiltration. This tumor proved to be clinically benign. x 75, x 125, x 125. (S. Warren and O. Gates, Boston)



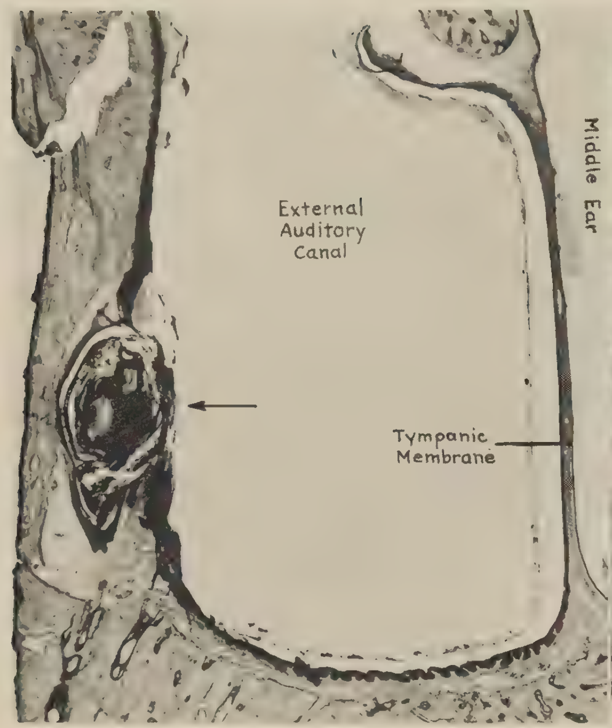
Ceruminal adenoma from dog. x 125. (S. W. Stiles, Portland, Maine)



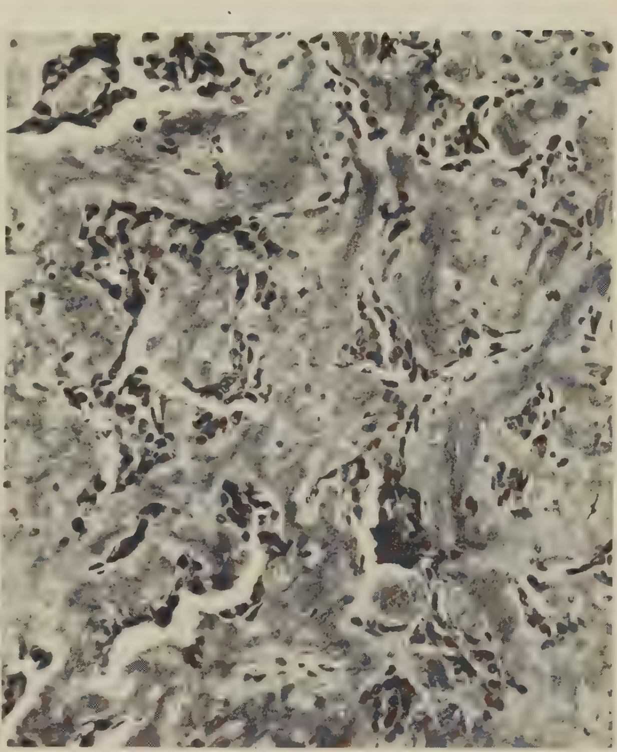
Ceruminal tumor from cat, one year's duration. x 48. (R. F. Vigne, Sanford, Maine)

Ceruminal adenomas are relatively more common in dogs and cats. They are usually benign in these species and the general picture is like that of the tumor in man.

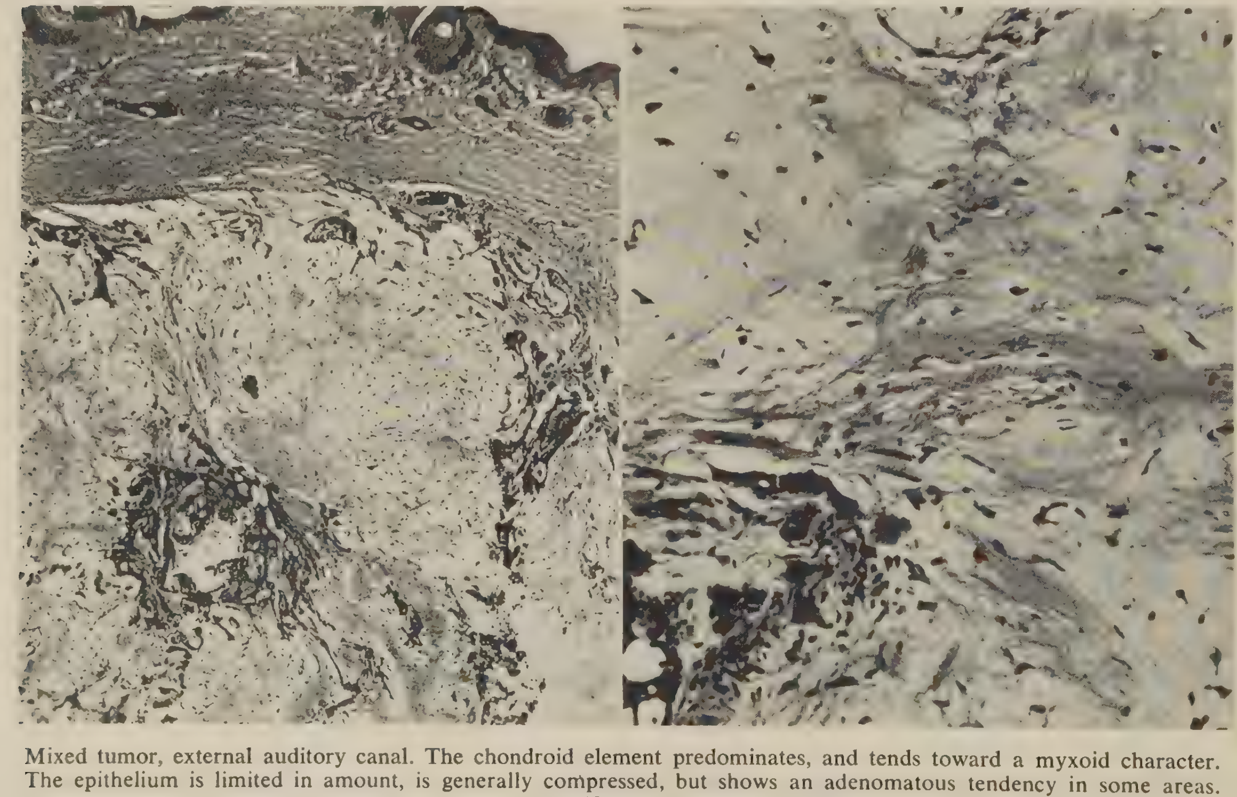
CHOLESTEATOMA–MIXED TUMOR, EXTERNAL AUDITORY CANAL



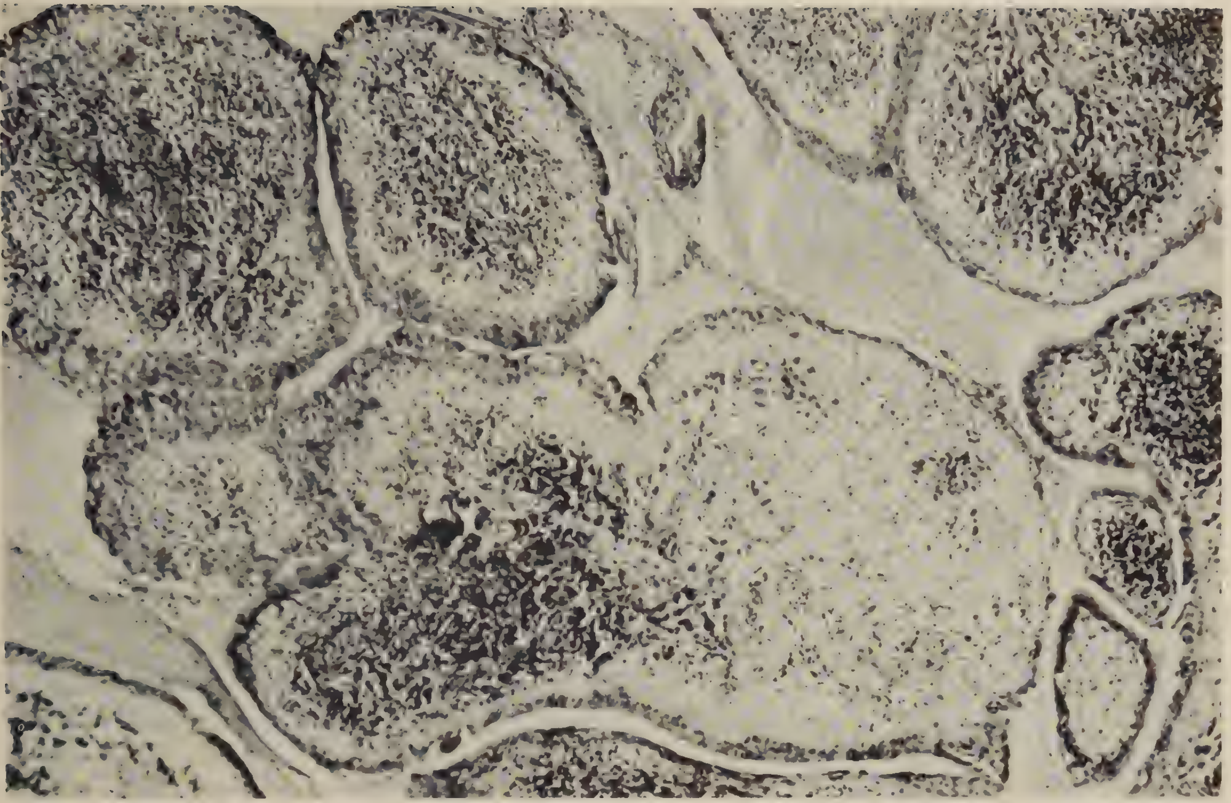
Cholesteatoma, left auditory canal, in a 35 year old woman who had chronic otitis media and cholesteatoma of the right ear. Arrow points to accumulation of keratin in a depression in bony canal. (F. Altmann and J. G. Waltner, New York)



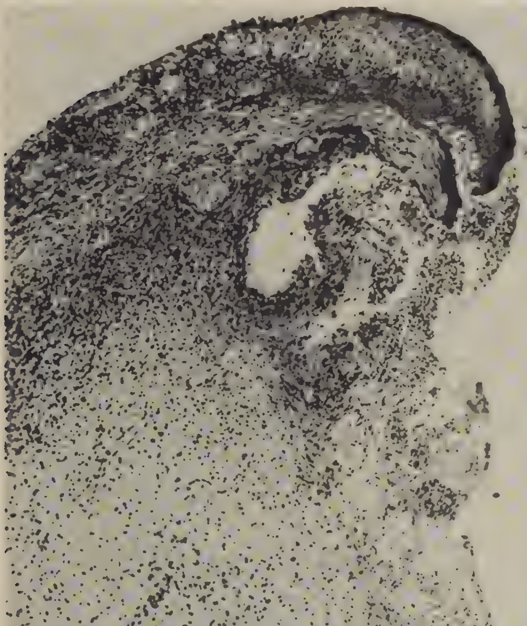
Mixed tumor, external auditory canal. Preponderance of chondroid element; attenuated epithelium. A rare tumor that develops from the glands of the lining epithelium. Such a tumor would be very difficult to eradicate. x 165.



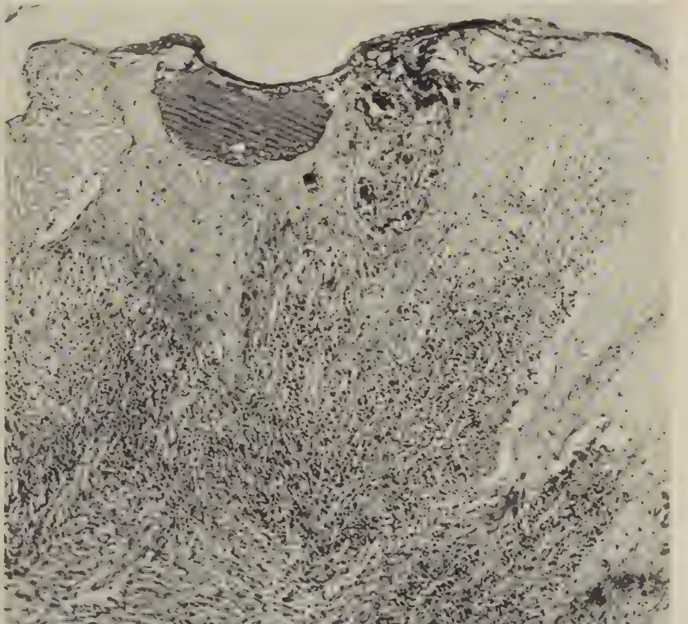
Mixed tumor, external auditory canal. The chondroid element predominates, and tends toward a myxoid character. The epithelium is limited in amount, is generally compressed, but shows an adenomatous tendency in some areas. x 48, x 165.



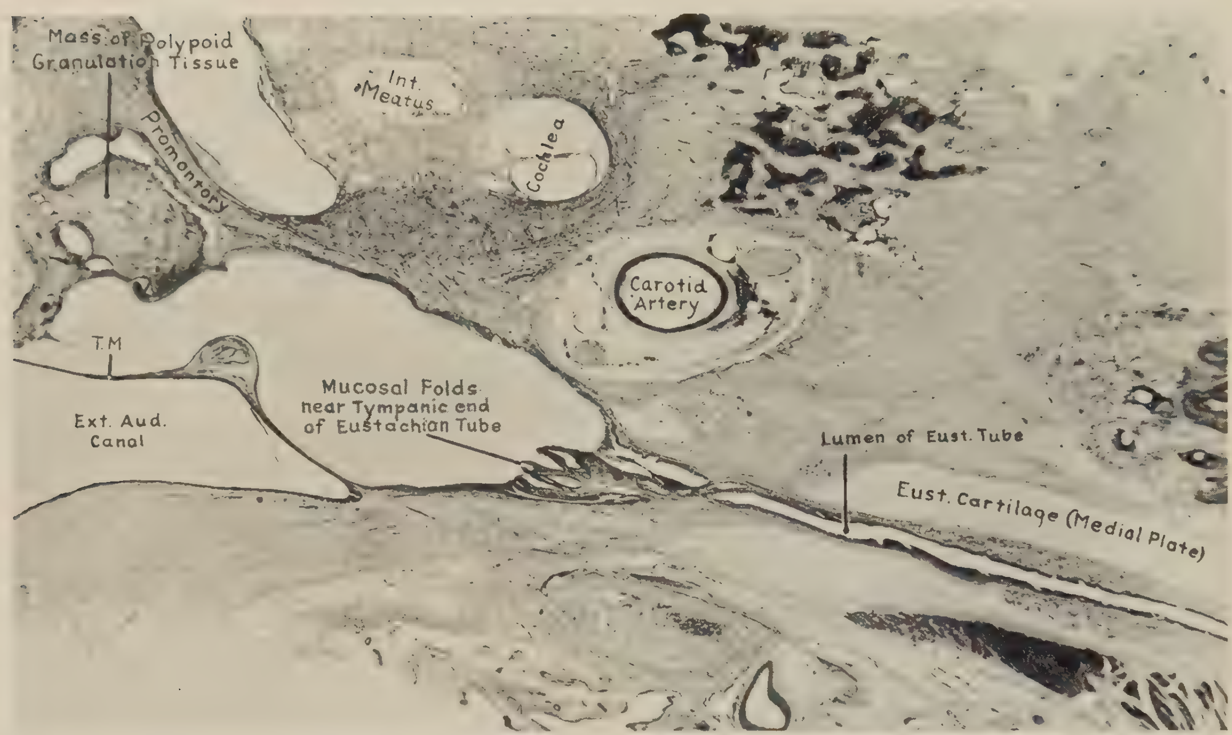
Papillary mass, removed from external canal as multiple polyps. It appears to have arisen from the canal lining rather than from the middle ear. (E. P. Fowler.)



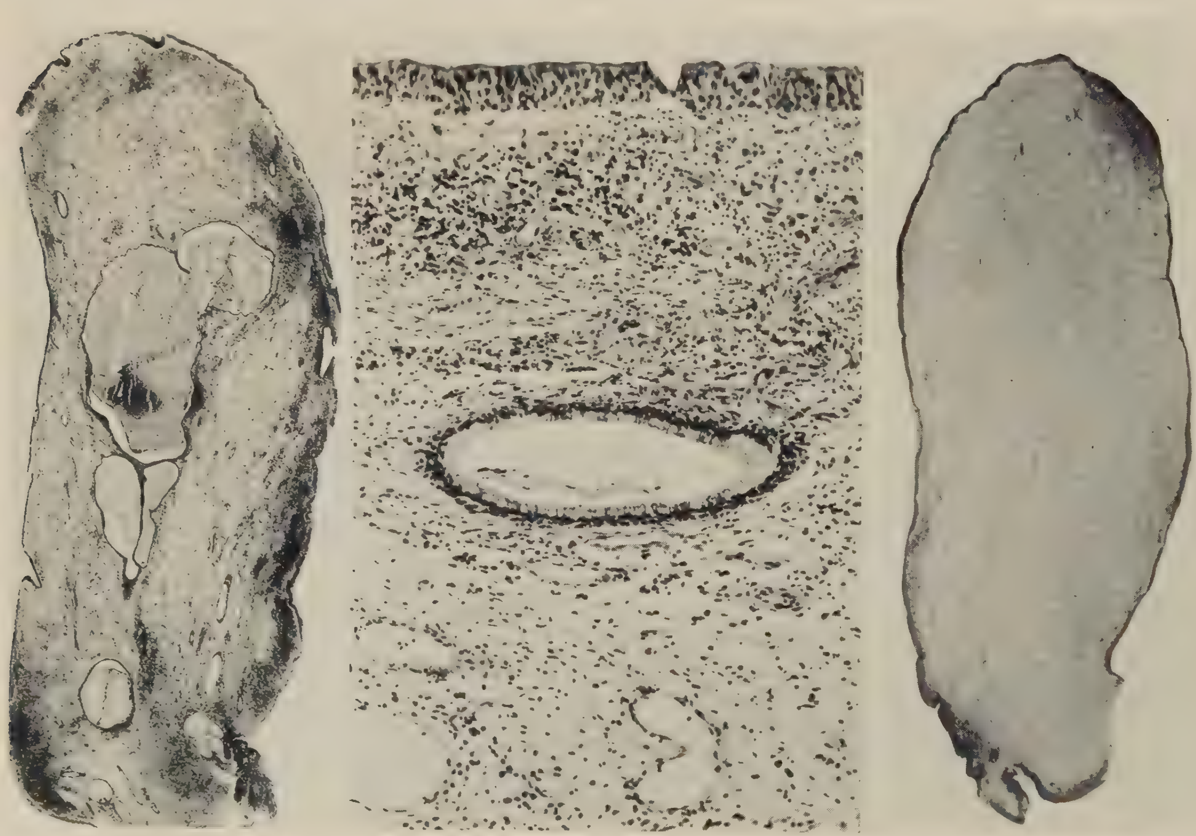
Otic polyp, arising from middle ear. Rather dense fibrous stroma. Surface largely ulcerated; squamous epithelium at top. x 70.



Otic polyp. The squamous epithelium shows pseudoepitheliomatous hyperplasia. Granulation tissue and exudate form the bulk of the mass. x 70.


Mass of Polypoid Granulation Tissue
Int. Meatus
Promontory
Cochlea
Carotid Artery
T.M
Ext. Aud. Canal
Mucosal Folds near Tympanic end of Eustachian Tube
Lumen of Eust. Tube
Eust. Cartilage (Medial Plate)

Horizontal section of temporal bone to show possible site of origin of otic polyps in chronic otitis media. Note mass of polypoid granulation tissue that could eventually extend through a ruptured external membrane. x 8.



A. **Polyp,** 1.5 x 0.5 cm., removed from patient on whom a mastoid operation had been performed four years previously. The cysts are dilated glands formed by inclusion of surface epithelium. x 10. B. The surface epithelium has retained its respiratory type. Granulation tissue and chronic exudate form the stroma. x 125. C. Another polyp, with edematous stroma and squamous epithelial covering; metaplasia from the original respiratory type. (E. P. Fowler, Jr.)

CHAPTER 32

MIDDLE EAR AND EUSTACHIAN TUBE

The **tympanic cavity** is a flattened multilocular space in the temporal bone, terminating at the inner end in the funnel-like constriction that forms the orifice of the eustachian tube, and at the outer end in the mastoid antrum. It is shielded from without by the **membrana tympani.** In the young infant the external tympanic membrane is round and in the adult it is elliptical, measuring 8 by 9 mm. It is thicker in infants than in adults and slants more towards the horizontal. The adult membrane is 0.1 mm. in thickness.

The bony ring — annulus — is always incomplete, leaving the notch of Rivinus in its upper anterior segment. It is at this point that the loose portion of the membrane (membrana flaccida) is attached. This is Shrapnell's membrane. There is scarcely any fibrous layer in this portion. The membrane otherwise is composed of three layers: the external or stratified squamous epithelium, the middle fibrous layer, and the internal mucous membrane. The external layer is easily detached, but the internal layer is intimately bound to the connective tissue. The stratified squamous epithelium is continuous with that of the skin of the external auditory canal. The middle fibrous layer consists of an external radiating, and an internal circular formation of fibers. It becomes thicker at the margin of the membrane. The internal mucous membrane layer is continuous with the lining of the tympanum and is covered with flattened cuboidal cells. There is a tunica propria that is a continuation under each layer of epithelium, containing the blood vessels and lymphatics.

The membrane shares in any inflammatory process of the middle ear, and the external surface may be involved by infections of the external canal or by trauma, directly through the canal in the case of foreign bodies, insects, impacted cerumen, or indirectly by blasts or sudden and extreme variations in atmospheric pressure. It is also ruptured by fractures of the bony wall. Rupture, the result of trauma, need not necessarily be complete, but may be limited to the separation of the layers by hemorrhage. In acute inflammation the epidermis becomes loosened, and in chronic inflammation, especially in eczema, it becomes hyperplastic.

MYRINGITIS BULLOSA is a complication of upper respiratory infections, including influenza and those caused by *Str. hemotolyticus* and the pneumococci. There is severe local pain and constitutional reaction from the infection. The walls of the external canal as well as the mucosa of the membrane become swollen to a degree that makes observation of the changes in the membrane difficult. Finally, the outer layers of membrane are dissected loose and the accumulation of serum produces the characteristic blebs. The condition usually subsides spontaneously and is aggravated by manipulation or medication.

The blood vessels of the tympanic membrane are not visible in the normal state but become evident from hyperemia in inflammation. Calcified and atheromatous foci in the mucosal layer and cystic pockets develop as results of chronic inflammation. The former are common and follow any type of inflammation of the membrane.

Inflammation with ulceration leads to formation of adhesions and bands between the tympanic membrane, ossicles, and adjacent walls. These adhesions are the cause of deafness when they interfere with the normal movements of the ossicles.

A serious complication of chronic otitis media with a marginal perforation of the tympanic membrane is the growth of squamous epithelium from the external canal into the middle ear. This can result in cholesteatoma.

Eustachian Tube (Auditory Tube).—The proximal portion of the eustachian tube is an extension of the middle ear through the temporal bone, and the pharyngeal cartilaginous part is an extension of the pharynx. With these two distinct anatomic and histologic divisions in mind, it is easier to picture the physiologic and pathologic implications. The tube is the only normal means of ventilation and drainage for the middle ear and it is the common path of direct invasion of the middle ear by infections. The development, anatomy, and histology of the eustachian tube have been reviewed in detail by Zöllner and Graves and Edwards. Its histology, however, has such an important bearing on the pathologic conditions of the tympanic cavity that it will be described here.

The tube is about 36 mm. long. It is the vestige of the first gill pouch and develops as a diverticulum from the foregut. In the embryo it opens onto the neck and occasionally in the adult there is a fistulous remains of this exterior position.

The tube begins as a narrowing of the tympanic cavity and becomes even narrower in its course through the petrous portion of the temporal bone for about 1.5 cm. The remaining two-thirds of the tube is a slit-like crevice partially surrounded by the eustachian cartilage. The tube is its narrowest at the isthmus where osseous and cartilaginous portions join. In old age, calcification of the cartilage at the isthmus occasionally occurs. Contrary to the usual diagrams the tube does not leave the middle ear at the level of the floor; its orifice is at the level of the upper half of the ear drum. In poorly pneumatized bone it may be so high as to be separated from the middle fossa of the skull by only a thin bony covering. The pharyngeal opening is about 15 mm. lower than the isthmus.

Pneumatization of the petrous bone may extend below the tube or completely surround it with air cells that are often lined with pseudostratified columnar epithelium. There is a close relationship between these cells about the bony parts of the canal and the veins and nerves surrounding the internal carotid artery.

There are two muscles of primary importance to the physiology of the tube: the TENSOR VELI PALATINI, which arises from the scaphoid fossa, the spine of the sphenoid, and then joins the muscle of the opposite side to form part of the soft palate. Its function is to open the mouth of the tube. The other muscle, the LEVATOR VELI PALATINI, arises from the base of the petrous portion of the temporal bone and also joins with its fellow on the opposite side to help form the soft palate. It probably functions directly to assist in opening the tube. The PHARYNGOPALATINUS MUSCLE—the posterior pillar of the fauces—has some indirect influence on the tubal orifice. Yawning and swallowing bring into play these muscles and thus assist in the ventilation of the tympanum. The cartilaginous part of the tube is subjected to the movements of the attached muscles and for this reason develops longitudinal folds. The osseous portion, on the other hand, is smooth, and the mucous membrane fuses with the periosteum forming a mucoperiosteum which resembles the lining of the ethmoidal sinuses.

The MUCOUS MEMBRANE OF THE EUSTACHIAN TUBE is a direct continuation of the nasopharyngeal mucous membrane. At the pharyngeal orifice it is thick and always contains a great many mixed serous and mucous glands, whose openings may sometimes be distinguished with the naked eye. From the pharyngeal orifice upward, the mucosa becomes more and more attenuated. The floor of the tube contains a rich network of lymphatic channels, nerves, and blood vessels.

The EPITHELIUM OF THE TUBE is of the pseudostratified, ciliated columnar type. Henle (1866) was the first to determine that the propulsive effect of the cilia is from the tympanic cavity toward the pharynx. In general two rows of nuclei appear in the epithelium. The nuclei of the ciliated columnar cells are oval in form and their position varies somewhat within the epithelium so that an irregular line of oval nuclei is seen above a layer of round nuclei which belong to the basal cells. The bulky end of the columnar cell contains a considerable quantity of cytoplasm which increases in amount and becomes pale when mucinous degeneration begins. Under normal conditions the columnar cells adhere to the basal epithelium, but during acute inflammation they loosen and break away, leaving the basal cells to regenerate a new epithelial covering.

The epithelium of the auditory tube stands out in sharp contrast to that of the surrounding paratubal pneumatic spaces. The epithelium within the petrous cells is so attenuated that it is relatively inconspicuous. It consists normally of only a single flat layer of cells, but with inflammatory processes these may become pseudostratified columnar.

Two clearly differentiated layers of submucous connective tissue are found, (1) the tunica propria, a superficial areolar layer of loose connective tissue, and (2) the deep layer (perichondrial or periosteal) formed by a dense deposit of white fibrous connective tissue. Between the two layers is a variable intermediate zone which often shows a gradual transition from loose to compact tissue. In some cases there is a sharp delineation. The tunica propria is more closely knit and the fibers are more collagenous than those of the paranasal sinuses. During otitis media the superficial layer of stroma is infiltrated with leukocytes and presents considerable swelling which throws the lining into polypoid folds, especially at the middle ear end of the tube.

Submucous glands are present in large numbers in the middle third of the tube but no lymphoid tissue is found in this region under normal conditions. The posterior lip of the pharyngeal orifice is a common site for lymphoid tissue and cicatricial bands which extend across the fossa of Rosenmüller. The anterior lip may be blocked by hypertrophied lymphoid tissue as well as by redundant turbinate tissue, bands and adhesions to the septum or to the turbinates.

Few pathologic changes other than inflammatory reactions in the eustachian tube are of practical importance. Such reactions are continuous with inflammations of the nasopharynx and of the tympanum and may be likened to those of the paranasal sinuses. Catarrhal tubotympanitis is more common than is generally supposed. Normally the tube lumen is perfectly clean and the mucosa shows no evidence of epithelial reaction or any exudate. The most constant and sometimes the only visible changes in catarrhal tubotympanitis are degeneration of the epithelium and discharge of an abnormal quantity of mucus or mucopus.

The eustachian tube is involved in every case of otitis media, with irregularity of the epithelium one of the first signs of inflammation. Chronic tubotympanitis creates lymphocytic infiltration which may be focal or diffuse, sometimes throwing the mucous membrane into papillomatous masses. These structures may assume the form of lymphatic nodules that result in obstruction. The only lymphoid tissue normally present in the eustachian tube is near the orifice, and that only during the first few months of life. This is the tubal tonsil. When it occurs later it is considered pathologic.

Mucopurulent catarrh of the tube is often observed in the healing stages of acute upper respiratory infections. The mucous membrane is swollen and hyperemic. The surface is covered with exudate which is mostly epithelial debris and mucus. Allergic tubotympanitis is fairly common and can be differentiated if other forms of inflammation are not present due to secondary factors. The chief clinical findings are swelling and tumescence of the orifice of the tube, associated with allergic inflammation of the nose and paranasal sinuses.

The tube may become obstructed by long continued or repeated attacks of nasopharyngitis. The obstruction may be due to hyperplasia of the lymphatic tissue about the orifices or there may be polypoid scar-tissue adhesions at either end of the tube. Occasionally, especially if there has been excessive trauma from bougienage, there may be similar strictures anywhere along the course of the tube. In the chronic granulomatous inflammations, particularly syphilis, there may be scarring with resulting stenosis.

The use of direct radium applications to the orifices of the eustachian tubes of aviators during the war to reduce the incidence of aerotitis media was viewed with some concern by otolaryngologists and radiologists. It was thought that not only the surrounding lymphatic tissue elements would be reduced but that there might be a deleterious effect on the mucous glands of the tube, possible scarring, and reaction in the mucosal epithelium. However, studies by Crowe and his associates had indicated the value of similar treatment in children, and neither he nor Fowler observed untoward results among military personnel so treated during World War II. Since acute nasopharyngitis and otitis cause temporary exacerbations of the tubal symptoms, radium should not be employed until such inflammations subside. Fowler warned against repeated irradiation, pointing out that one treatment will profoundly affect the sensitive lymphatic tissue. The histologic details of the reaction are illustrated in the section on the effects of irradiation.

Tympanic Cavity.—The inner wall of the tympanic cavity is of particular importance because of the two fenestra separated by the bony promontory. The oval window into which the foot of the stapes articulates communicates with the vestibule. Somewhat lower and mesially the round window is closed by the secondary tympanic membrane. The histology of the secondary membrane is important in connection with the transmission of infections from the middle ear into the labyrinth. Its outer surface is covered by a well vascularized extension of the middle-ear mucosa. The inner surface is thin and poorly vascularized. Between the two mucosal layers is a membrana propria of elastic and fibrous tissues. This membrane differs from the external tympanic membrane in that the former is thicker in the middle than peripherally. Infections in the middle ear, therefore, gain access through this looser periphery, and the delicate inner mucosal surface shows damage before the middle ear surface. The membrane can remain intact after the establishment of labyrinthitis and interfere with drainage. The oval window is filled by the foot plate of the stapes. This, too, can be attacked by inflammatory processes and break down to allow invasion of the labyrinth. Likewise the annular ligament surrounding the foot plate of the stapes can be invaded. The structure of the ligament is similar to that of the secondary tympanic membrane except that its connective tissue layer is much thicker and includes elastic fibers.

There are three divisions of the tympanic cavity: 1. The EPITYMPANIC SPACE or ATTIC which lies above the upper margin of the external tympanic membrane. It is occupied by the incus and the head of the malleus. Prussak's space, in the lower outer portion, is bounded by the internal aspect of Shrapnell's membrane with the neck of the malleus forming its posterior border. 2. The ATRIUM, between the levels of the upper and lower borders of the tympanic membrane, is bounded internally by the promontory. 3. The HYPOTYMPANIC SPACE lies below the level of the membrane.

The roof of the tympanic cavity is the TEGMEN TYMPANI that forms part of the floor of the middle fossa of the skull. There is almost always a number of air cells in the roof and in the floor of the middle ear, so that its precise dimensions are impossible to estimate.

Orientation in the anatomic details of the tympanum and other portions of the temporal bone can be obtained by a study of the illustrations.

The MUCOUS MEMBRANE OF THE TYMPANUM is a modified form of respiratory epithelium and in the adult is very thin, no more than 0.05 mm. in some areas. The cells are lower than those of the respiratory tract and are normally ciliated only in the tubal orifice. Cilia are absent over the promontory, the ossicles, the tympanic membrane and aditus ad antrum. The epithelium near the opening of the eustachian tube and along the floor of the anterior part of the cavity is pseudostratified columnar and gradually becomes lower in the superior and middle part of the cavity. The connective tissue forms a delicate mucoperiosteum which is well developed only in certain areas over the promontory. There are no glands in the middle ear except for a few simple ones that may appear near the openings of the tubes. In spite of this, a mucoid discharge comes from the epithelium under conditions of inflammation.

The ligaments and folds in the mucosa in the attic often are thickened and obstruct drainage from the attic and antrum of the mastoid. Embryonic gelatinous connective tissue sometimes appears in the attic and bands may be present between the tympanic membrane and the inner wall of the ear. Strings of delicate tissue also are found around the oval window and sometimes in the round window. These tissues favor the formation of adhesions and when they become inflamed the hyperplasia is sufficient to interfere with the function of the ossicles.

The lining membrane in the newborn and in infants is remarkable for its greater thickness and vascularity. The infantile tympanic cavity is filled with embryonic conective tissue which is absorbed shortly after birth and within six or eight weeks should appear as a thin membrane. It may remain thickened, especially in the attic, to create more obstruction than is seen in the normal adult ear.

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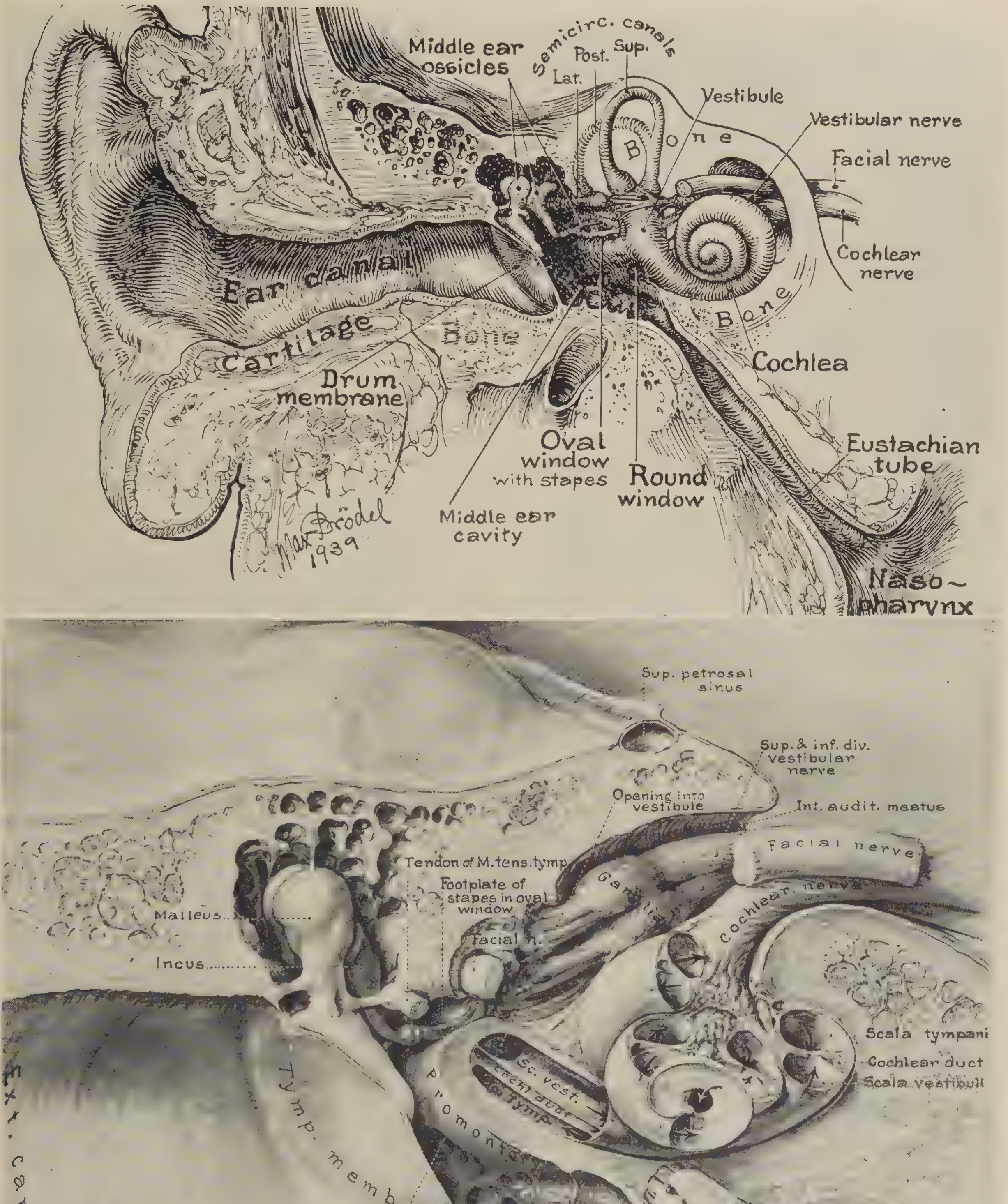
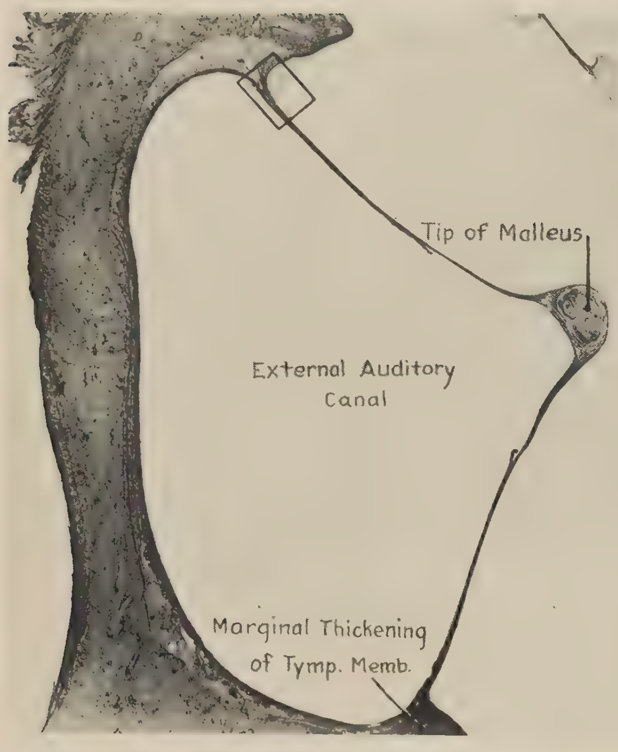
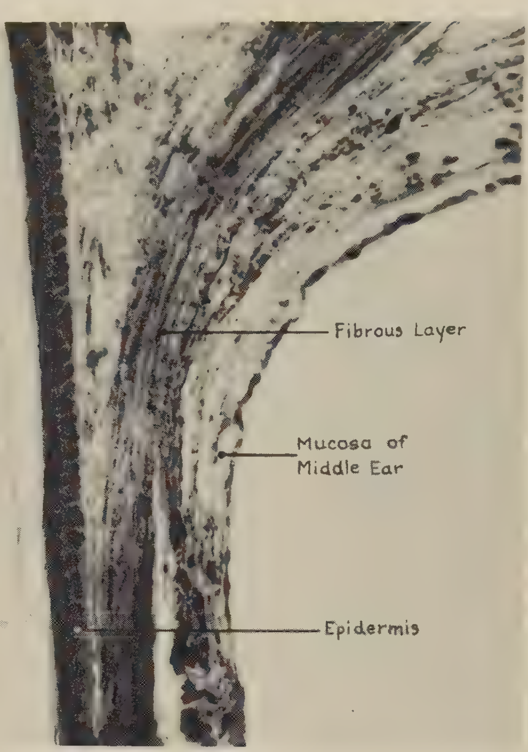

Middle ear ossicles
Semicirc. canals
Post.
Sup.
Lat.
Vestibule
Vestibular nerve
Bone
Facial nerve
Cochlear nerve
Ear canal
Cartilage
Bone
Drum membrane
Bone
Cochlea
Oval window with stapes
Round window
Middle ear cavity
Eustachian tube
Naso-pharynx
Max Brödel 1939
Sup. petrosal sinus
Sup. & inf. div. vestibular nerve
Opening into vestibule
Int. audit. meatus
Facial nerve
Tendon of M. tens. tymp
Footplate of stapes in oval window
Malleus
Incus
Ganglion
Cochlear nerve
Facial n.
Scala tympani
Cochlear duct
Scala vestibuli
Sc. vest.
Cochl. duct
Sc. tymp.
Promontory
Tymp. memb.
Ext. canal
Round window
Middle ear cavity
Eustachian tube
M. tensor tympani

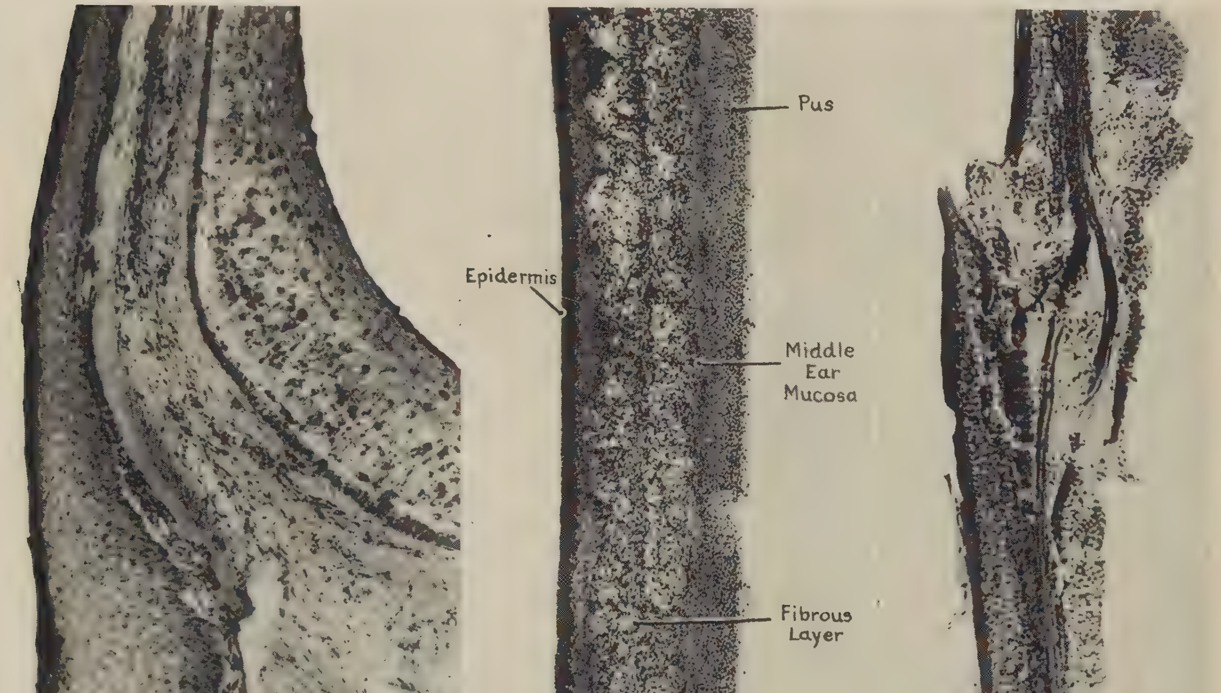
These drawings for anatomic orientation by Max Brödel were completed by P.D. Malone, and are reproduced here from the originals by courtesy of Dr. Stacy R. Guild. They were included in "Three Unpublished Drawings of the Anatomy of the Human Ear," W.B. Saunders Company, Philadelphia, 1946.


Tip of Malleus
External Auditory Canal
Marginal Thickening of Tymp. Memb.

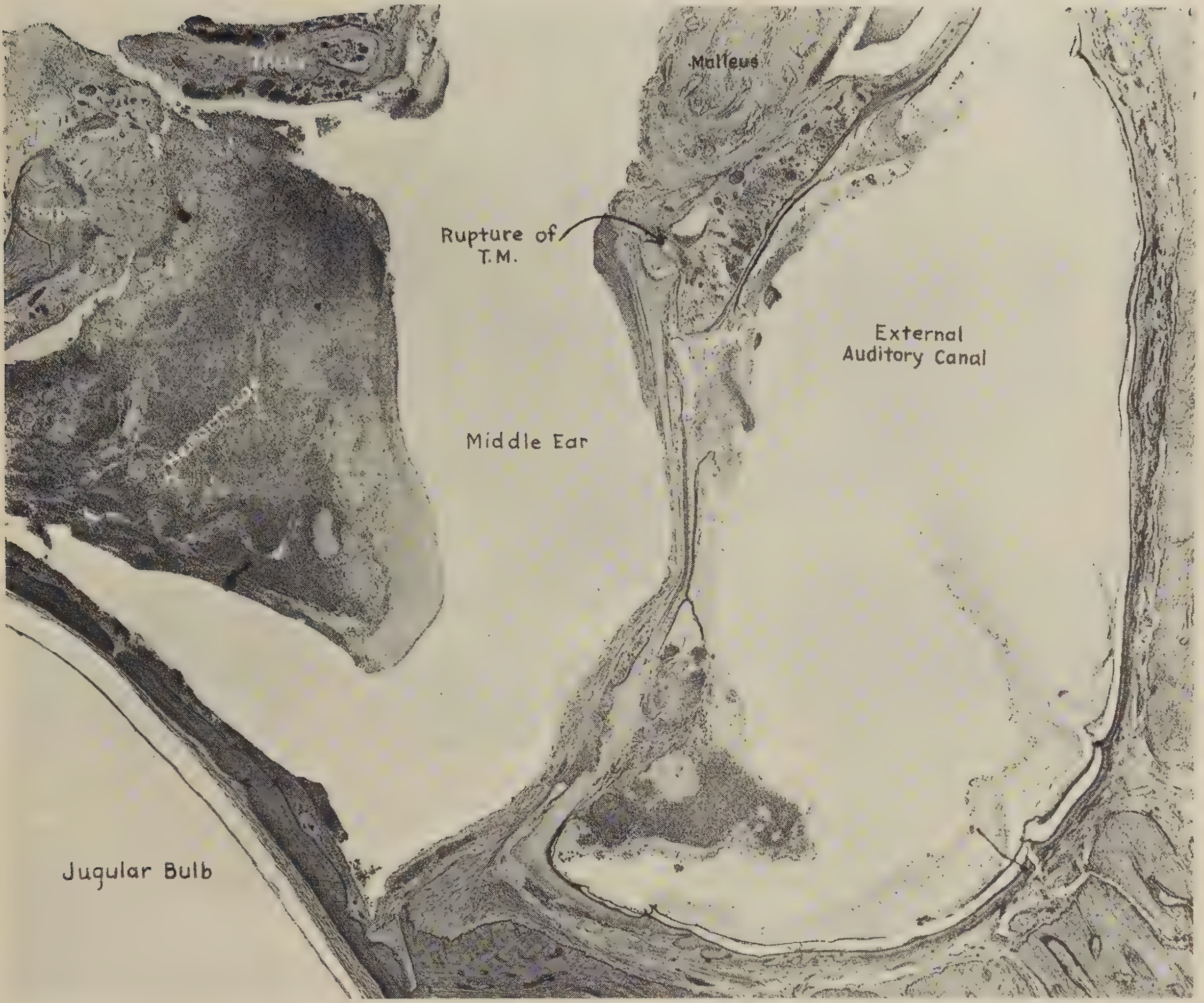
Relatively normal membrane: Section for orientation. x 12.


Fibrous Layer
Mucosa of Middle Ear
Epidermis

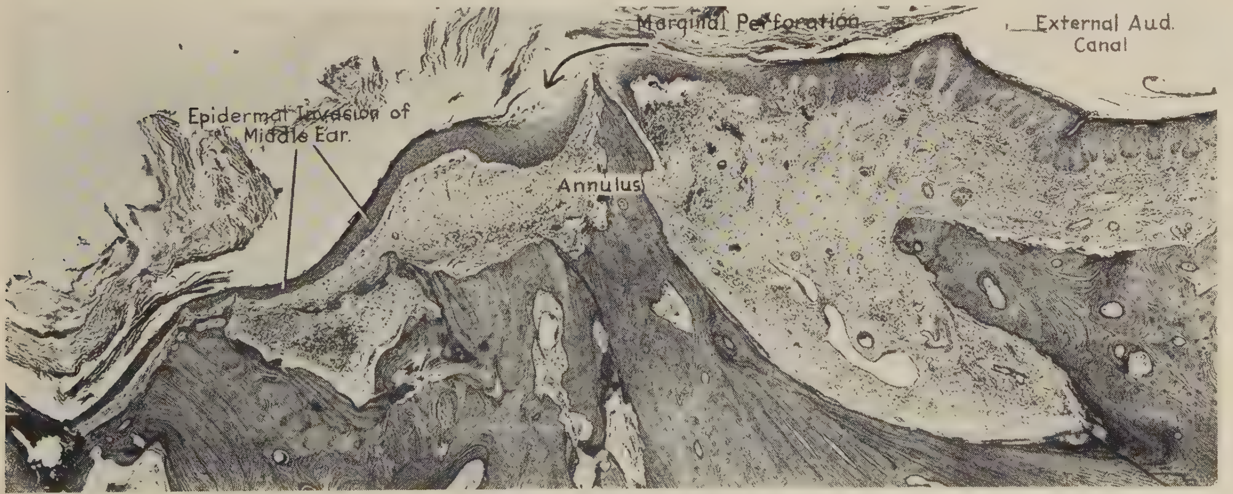
Details of blocked area in previous figure. Thicker than normal from an inflammatory reaction. x 350.


Pus
Epidermis
Middle Ear Mucosa
Fibrous Layer

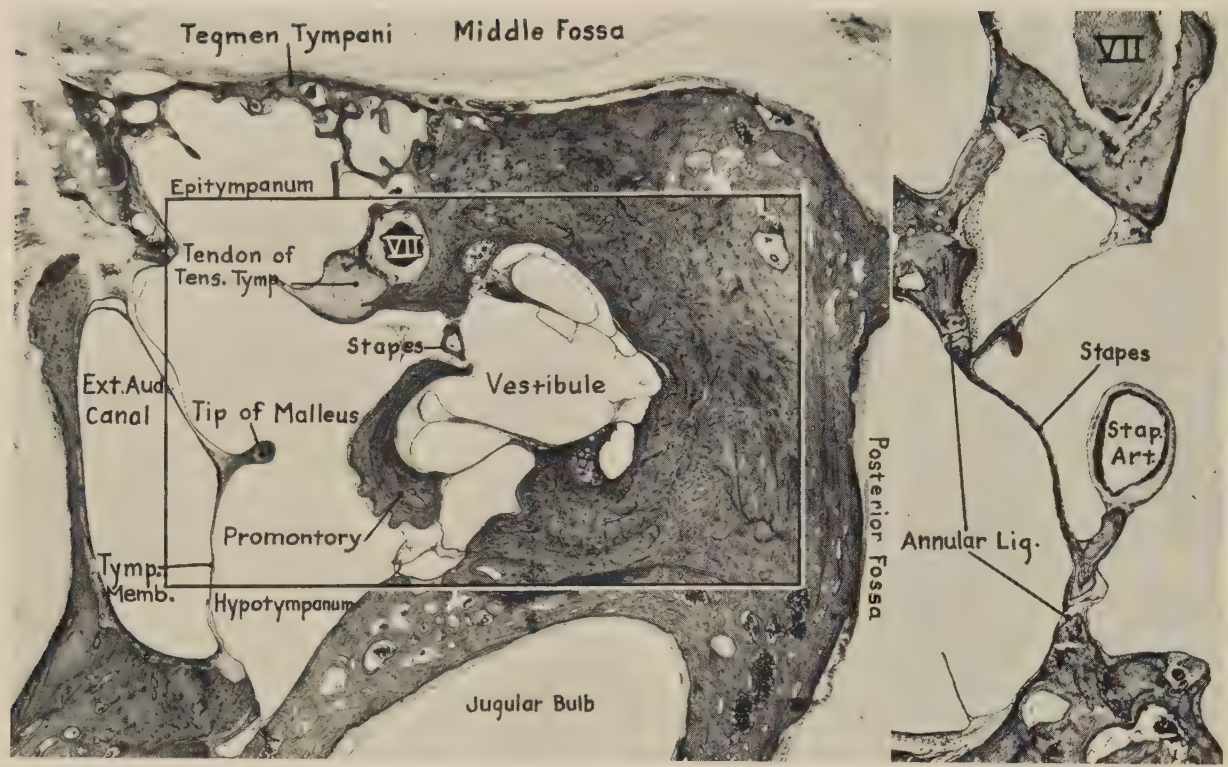
Otitis media. A. Lower margin of membrane greatly thickened by edema of fibrous layer and by exudate on middle ear mucosa. Squamous epithelium of external surface is thickened. x 100. B. Middle portion of membrane thickened by exudate. C. Site of rupture of membrane. Fibrous layer necrotic, internal and external mucosae ulcerated. (G. Kelemen, Boston)


Malleus
Rupture of T.M.
External Auditory Canal
Middle Ear
Jugular Bulb

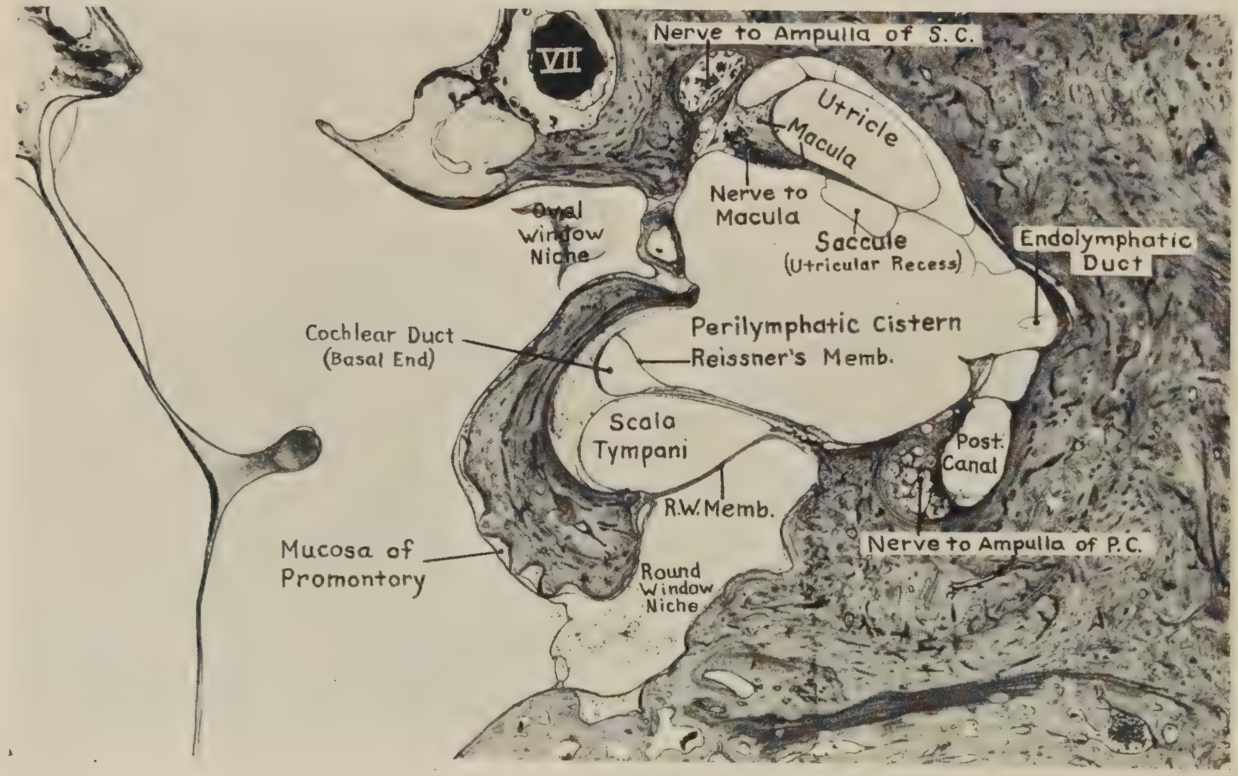
Traumatic rupture, tympanic membrane. Concussion from high explosive shell ruptured the membrane and induced a large hemorrhage into the middle ear. x 20. (Mosher Laboratory, Boston.)


Marginal Perforation
External Aud. Canal
Epidermal Invasion of Middle Ear.
Annulus

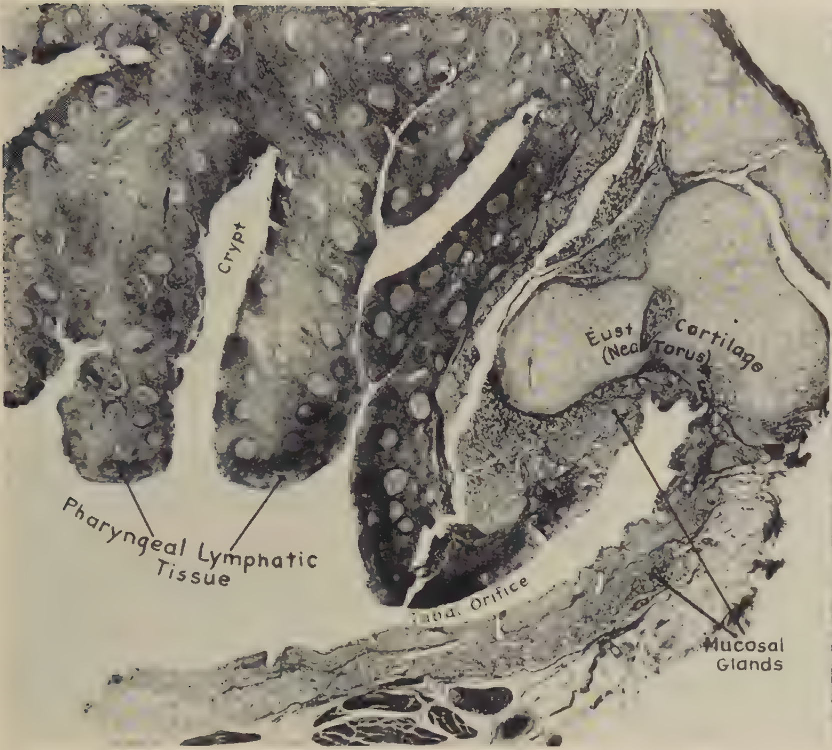
Epidermidization of middle ear, following perforation of membrane. From a 56 year old man who had otitis media for 13 years. The membrane was practically destroyed. x 20. (H. A. Kuhn, Hammond, Ind.)


Tegmen Tympani
Middle Fossa
Epitympanum
Tendon of Tens. Tymp.
VII
Stapes
Vestibule
Ext. Aud. Canal
Tip of Malleus
Promontory
Tymp. Memb.
Hypotympanum
Posterior Fossa
Jugular Bulb
VII
Stapes
Stap. Art.
Annular Lig.

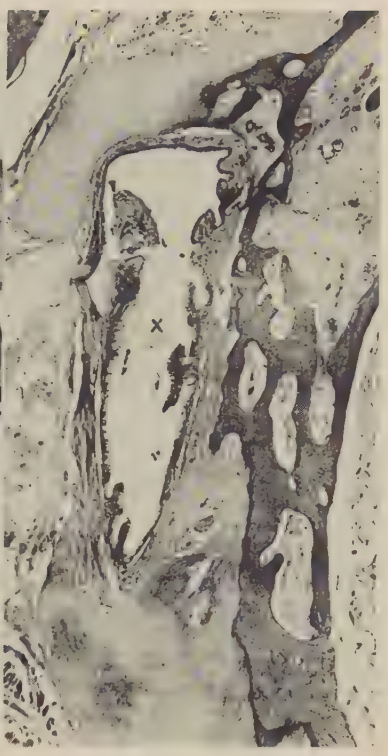
Relatively normal small middle ear, coronal section, for orientation. Persistent stapedius artery in head of stapes, a congenital anomaly (at right).


VII
Nerve to Ampulla of S. C.
Utricle
Macula
Nerve to Macula
Oval Window Niche
Saccule (Utricular Recess)
Endolymphatic Duct
Perilymphatic Cistern
Cochlear Duct (Basal End)
Reissner's Memb.
Scala Tympani
Post. Canal
R.W. Memb.
Mucosa of Promontory
Round Window Niche
Nerve to Ampulla of P.C.

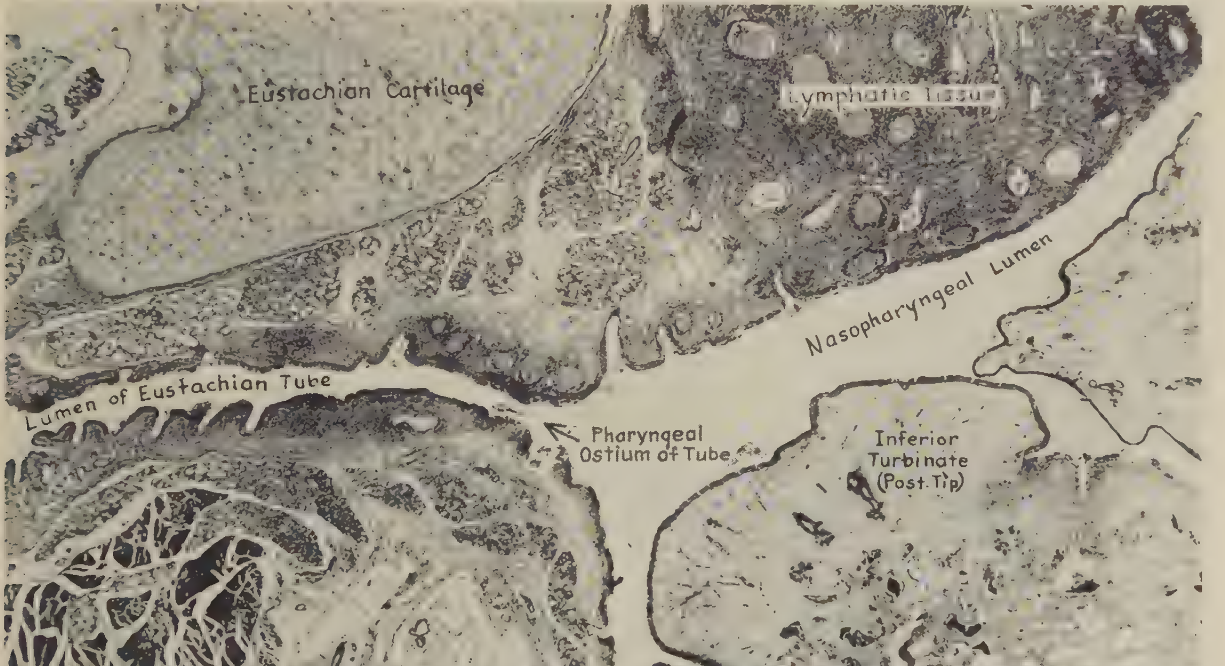
Higher magnification of the blocked area in large figure above.


Crypt
Eust Cartilage (Near Torus)
Pharyngeal Lymphatic Tissue
Tubal Orifice
Mucosal Glands

Pharyngeal end of eustachian tube from a young adult male. The pharyngeal lymphatic tissue is more abundant than normal and is encroaching on the tubal orifice.

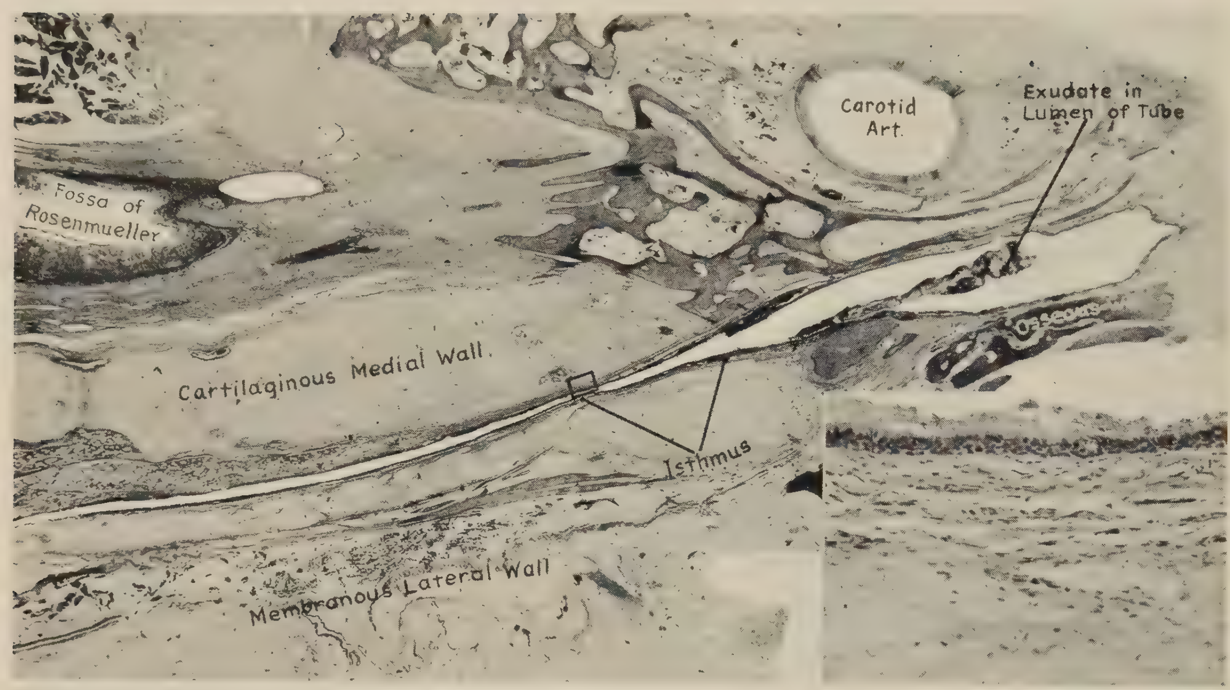


Cross section of tube at osseo-cartilaginous junction near isthmus.

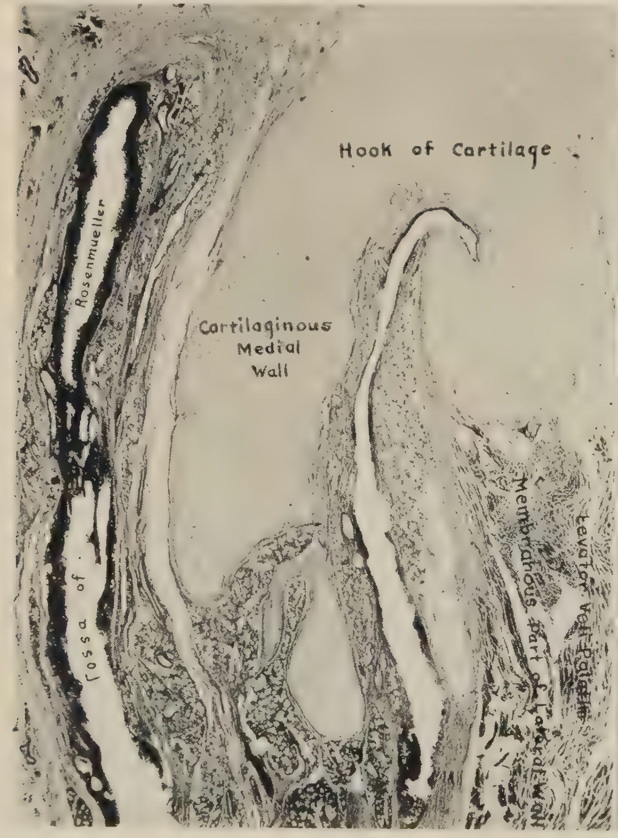

Eustachian Cartilage
Lymphatic Tissue
Nasopharyngeal Lumen
Lumen of Eustachian Tube
Pharyngeal Ostium of Tube
Inferior Turbinate (Post. Tip)

Orifice of eustachian tube from a young adult male on a different plane than in larger figure above. Tip of turbinate and fragment of polyp (right) indicate a significant hyperplastic rhinitis.

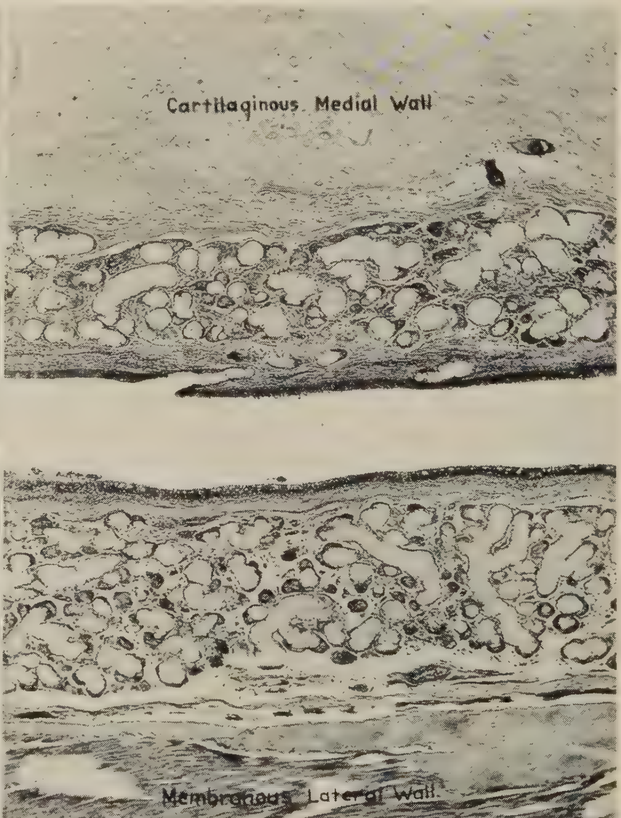
Note: These sections are from temporal bones sent to the AFIP by Dr. E. P. Fowler, Jr., from European Theater during World War II.


Fossa of Rosenmueller
Carotid Art.
Exudate in Lumen of Tube
Osseous
Cartilaginous Medial Wall
Isthmus
Membranous Lateral Wall

Anterior (medial) and posterior (lateral) portions of tube. Note exudate in distal portion. x 48. Inset shows the mucosa of blocked portion of isthmus. x 125.


Hook of Cartilage
Rosenmueller
Fossa of
Cartilaginous Medial Wall
Membranous Part of Lateral Wall
Levator Veli Palatini

Section of distal end of tube in another plane to show hook of cartilage. Levator veli palatini muscle at right. (H. Semenov)


Cartilaginous Medial Wall
Cartilaginous Medial Wall
Membranous Lateral Wall

Mucosa of tube near pharyngeal orifice. Note abundance of mucous glands and absence of lymphatic tissue. x 48.

CHAPTER 33

OTITIS MEDIA

Otitis Media Neonatorum.—Inflammation in the ears of the newborn is partially the result of hyperplastic, poorly organized mucosa and, in a number of instances, of aspiration of amniotic fluid and its contents through the eustachian tube. When the placental circulation is interrupted, the resultant fetal asphyxia is sufficient to stimulate the fetal respiratory center and thus initiate premature respiratory movements *in utero*. As a consequence, vernix caseosa, epithelial cells, and amniotic fluid are aspirated and appear not only in the nose, mouth and lungs, but also in the upper respiratory tract and especially in the middle ear. Farber and Sweet found amniotic contents in the lungs of 88 per cent of 124 infants under five weeks of age.

The inflammation may be either catarrhal or exudative. In the former the middle ear contains mucoid material and the mucosa is further thickened by edema and a small amount of cellular exudate. Bacterial infections may take place shortly after birth and this may complicate the developmental processes, or pre-existing developmental defects can be the basis for the infection. The exudate is more cellular and purulent than in the catarrhal type and fills the middle ear, attic, antrum and mastoid cells. It can result in necrosis of the tympanic membrane and of some of the bony structures. This is particularly true in older children when otitis has been a complication of scarlet fever.

Acute Otitis Media.—Acute inflammation of the middle ear is one of the most common otologic conditions and is due to an infection that has ascended in or along the eustachian tube. The inflammation need not necessarily be purulent in type, but may consist of edematous thickening of the mucosa of the eustachian tube and middle ear and the accumulation of mucoserous fluid in the tympanic cavity. This fluid is evident through the congested tympanic membrane. A variety of organisms including streptococci may incite this mild form of infection and it may also be a complication of the exanthems, scarlet fever or measles. The commonest predisposing cause is interference with drainage through the eustachian tube, and this in turn is usually the result of large adenoids.

When the infection is by more virulent organisms of the pyogenic group, of which *Streptococcus hemolyticus* or one of the pneumococci are prominent offenders, the exudate is no longer of the seromucous type but is purulent. Wittmaack in 1906 described a form of acute otitis which he designated mucosus otitis, in recognition of the etiologic agent *Streptococcus mucosus*. It was distinguished by the alarming nature of its late manifestations in contrast to its early mild clinical aspect. Later work proved that the causative organism was indistinguishable from Pneumococcus type III and it appears in more recent literature under the term Pneumococcus III otitis. A study in 1942 by Carlens, in which all cases were proved bacteriologically, does not confirm Wittmaack's contention that this type of otitis occurs primarily in old age. Fifty-five per cent of Carlens' patients were less than 25 years of age. When compared with otitis of other etiologies, however, the Pneumococcus III form is relatively more common in patients over the age of 40. The idea that it was more frequent in the older group no doubt arose from the fact that serious complications are far more common than in the streptococcal form and the disease in the young is usually resolved without complication if secondary infection does not occur. The tympanic cavity fills with pus and the tympanic membrane bulges and is turgescent. The exudate tends to accumulate in the oval window and in the niche of the round window. The rapid desquamation of the epithelial cells and their degeneration gives rise to the so-called mucous globules. Relief from the accumulation of exudate is obtained spontaneously by erosion and rupture of the external tympanic membrane.

If drainage is not effected either spontaneously or operatively, the accumulating exudate extends farther into the pneumatized portions of the temporal bone. With the availability of the modern powerful antibiotics serious complications of otitis media have been greatly reduced.

During the acute phases there are marked changes in the epithelium of the mucosa. The cells become degenerated or necrotic, others fill with mucus, one or more layers of the cells may desquamate, and cilia may appear on cells not normally ciliated. If the infection is particularly virulent, ulceration of the entire thickness of the mucosa exposes the underlying bone to direct infection.

If drainage is established early and the infection is overcome, complete restoration of the mucosa is possible. If, however, the active inflammatory process persists until granulation tissue develops or there have been repeated infections with granulation tissue formation, serious adhesions result which interfere with the activity of the ossicles, including the articulation of the foot plate of the stapes with the oval window. Under these circumstances deafness may result. Another possible complication is the isolation and infection of the facial nerve through osteomyelitis and sequestration of the bony canal.

Under favorable circumstances, with proper treatment, the purulent exudate subsides in both the middle ear and mastoid. It may, however, become pocketed in the mastoid and persist after the middle ear becomes normal. The submucous tissue may continue to be swollen and infiltrated with round cells for an indefinite period. The clinical evidence of this condition is a clear serous material in the middle ear and mastoid cells, which is sterile but which may become reinfected when antibacterial agents are discontinued. Slight deafness and a cloudy appearance of some or all of the mastoid cells may be the only signs of persistent infection.

Chronic Otitis Media.—The transition of acute purulent otitis media into chronic otitis media is, as a rule, an insidious process which runs an indeterminate course with occasional exacerbations and remissions of inflammation. Many factors contribute to this pathologic picture. Prussak's space is involved early in childhood because of its relation to the ossicular ligaments and aditus ad antrum where persistent thickened membrane is most commonly found. The excessive thickening of this membrane impedes drainage. The retention of exudate and pus in the depressions of the tympanic cavity, petrosal cells, mastoid antrum and mastoid cells continues to act as a source of reinfection. On the other hand, another important factor is deficiency in the pneumatization of the temporal bone. This increases the difficulty of drainage and also the possibility of residual foci of infection. Clinical experience has demonstrated beyond doubt that a great many of the otologic problems in adults date from early childhood.

CHRONIC PURULENT OTITIS MEDIA in children produces more thickening of the mucosa than in adults. It is characterized by papillary formations sometimes located upon the bony spines that arise from the walls of the tympanic cavity. Such thickenings are most marked on the promontory, on the head of the stapes, on the tendon of the tensor tympani muscle and over the ridge of the facial nerve canal. The attic is completely filled with thickened tissue and the aditus ad antrum is practically obliterated, so that drainage from the mastoid antrum is almost at a standstill.

Microscopically, the proportion of lymphocytes in the exudate increases and these cells become more concentrated as the edema and congestion decrease. Projections of the mucosa from accumulation of chronic exudate and fibroblastic proliferation extend into the cavity. Granulation tissue replaces the mucosa over areas denuded by ulceration, and organization of hemorrhages, of fibrinous exudate and of points of contact between ulcerated surfaces produce adhesions. The bony walls may be involved and become necrotic with attempts at repair through osteoclasis and osteogenesis. All of these features may extend into the mastoid and labyrinthine capsule. Erosion of the bony canal for the facial nerve leads to facial paralysis. Erosion through the floor of the middle ear permits the infection to involve the jugular bulb, leading to thrombosis. The escape of purulent material through congenital defects in the bony walls of the middle ear is responsible for occasional direct intracranial infections.

In the opinion of Ojala chronic adhesive otitis will soon be the commonest disease of the middle ear leading to serious impairment of hearing. The modern antibacterial agents prevent the development of suppurative chronic otitis in most instances, but the adhesive form, which develops insidiously and clinically resembles otosclerosis, is a more difficult therapeutic problem.

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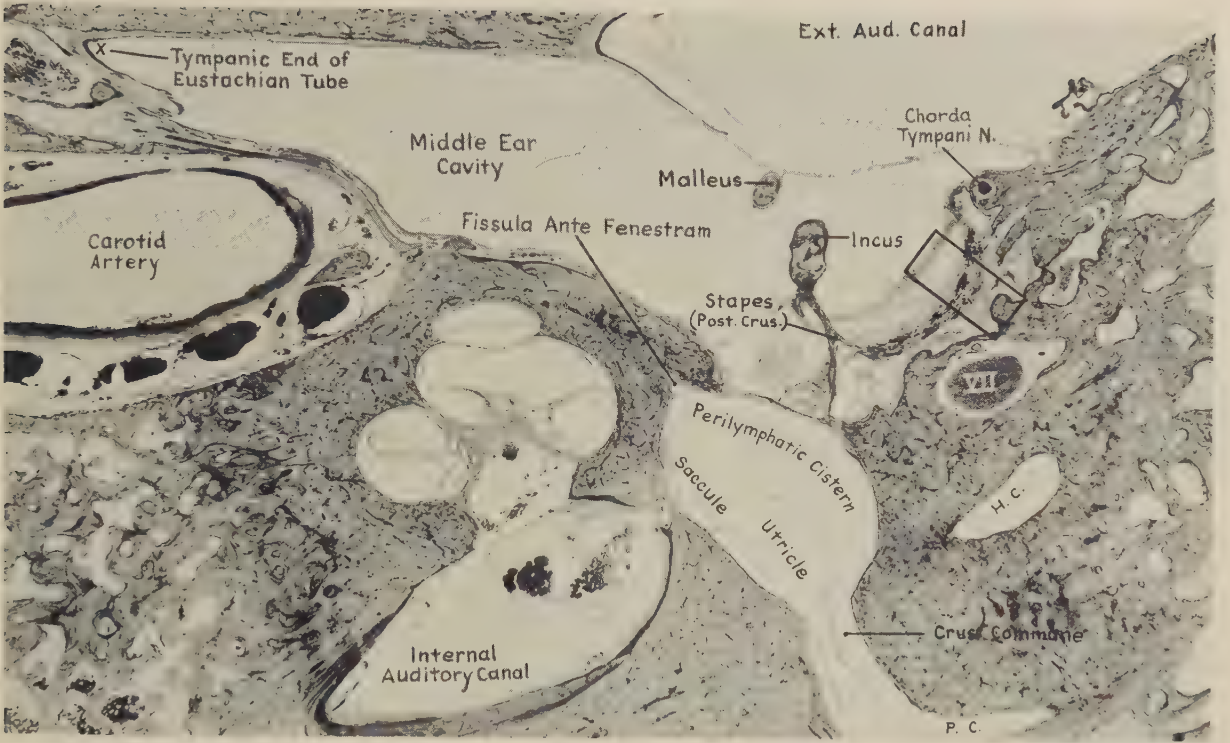
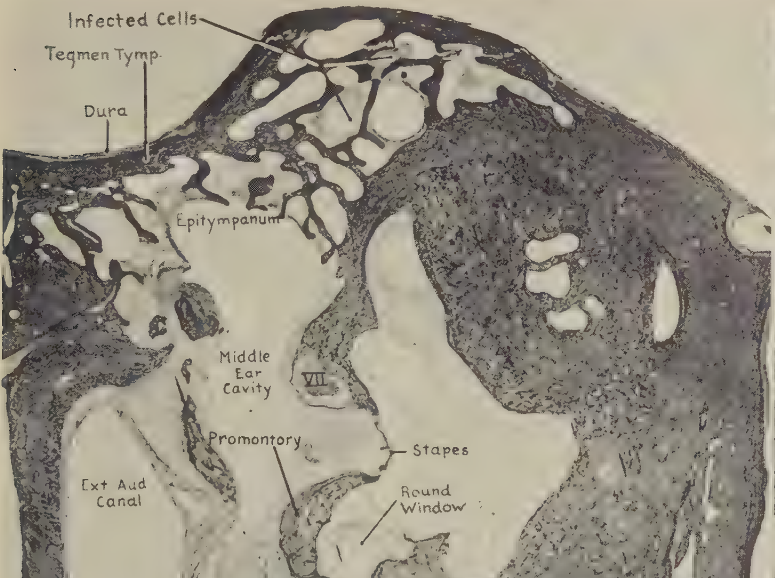
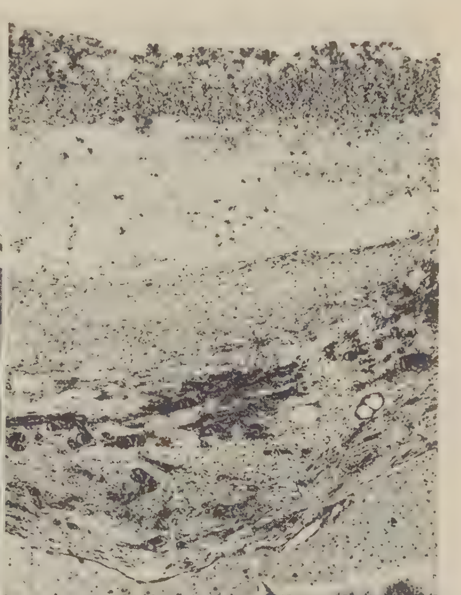

X
Tympanic End of Eustachian Tube
Ext. Aud. Canal
Middle Ear Cavity
Chorda Tympani N.
Malleus
Carotid Artery
Fissula Ante Fenestram
Incus
Stapes, (Post. Crus.)
VII
Perilymphatic Cistern
Saccule
Utricle
H. C.
Crus Commune
Internal Auditory Canal
P. C.

Otitis media, early, in a child. Roughly horizontal section of temporal bone. Exudate has accumulated about the oval window and ossicles. (E. P. Fowler, Jr., N. Y.).

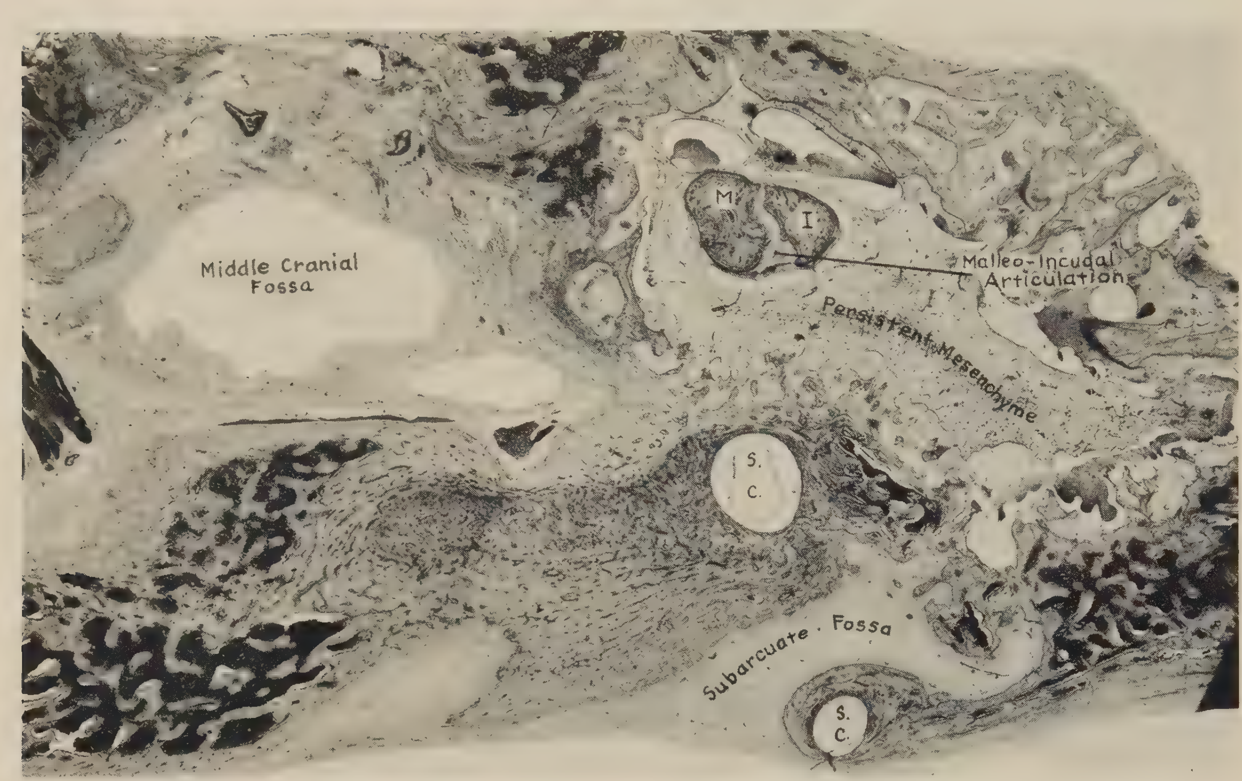

Infected Cells
Teqmen Tymp.
Dura
Epitympanum
Middle Ear Cavity
VII
Promontory
Stapes
Round Window
Ext Aud Canal
Tymp Memb.
Pus
Hypotympanum
Jugular Bulb

Otitis media, acute purulent, in a 35 year old Negro who died of pneumonia. Vertical section of temporal bone. Purulent exudate bathes all the surfaces of the middle ear and extends into attic and petrous air cells. (S. R. Guild.)

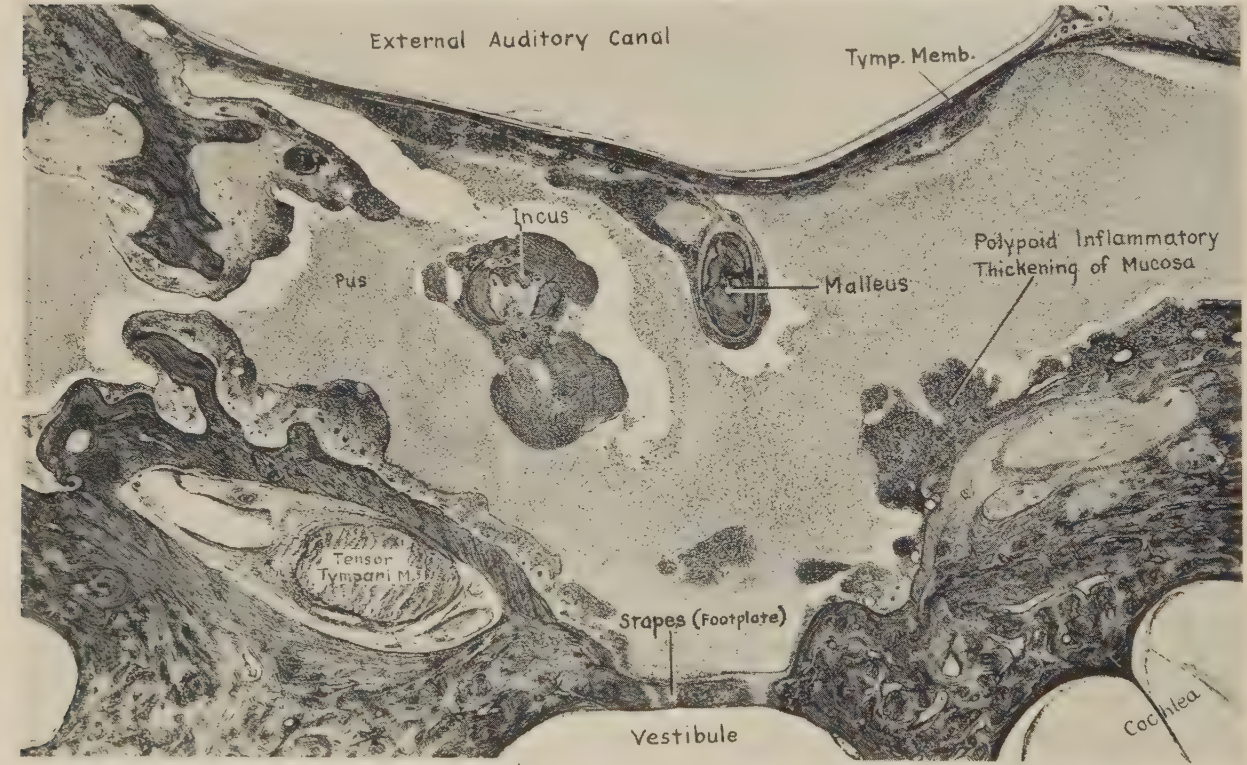


Detail of mucosal involvement in blocked area in section above. Mucosa greatly thickened by edema and purulent exudate. Epithelium at top. x 48.

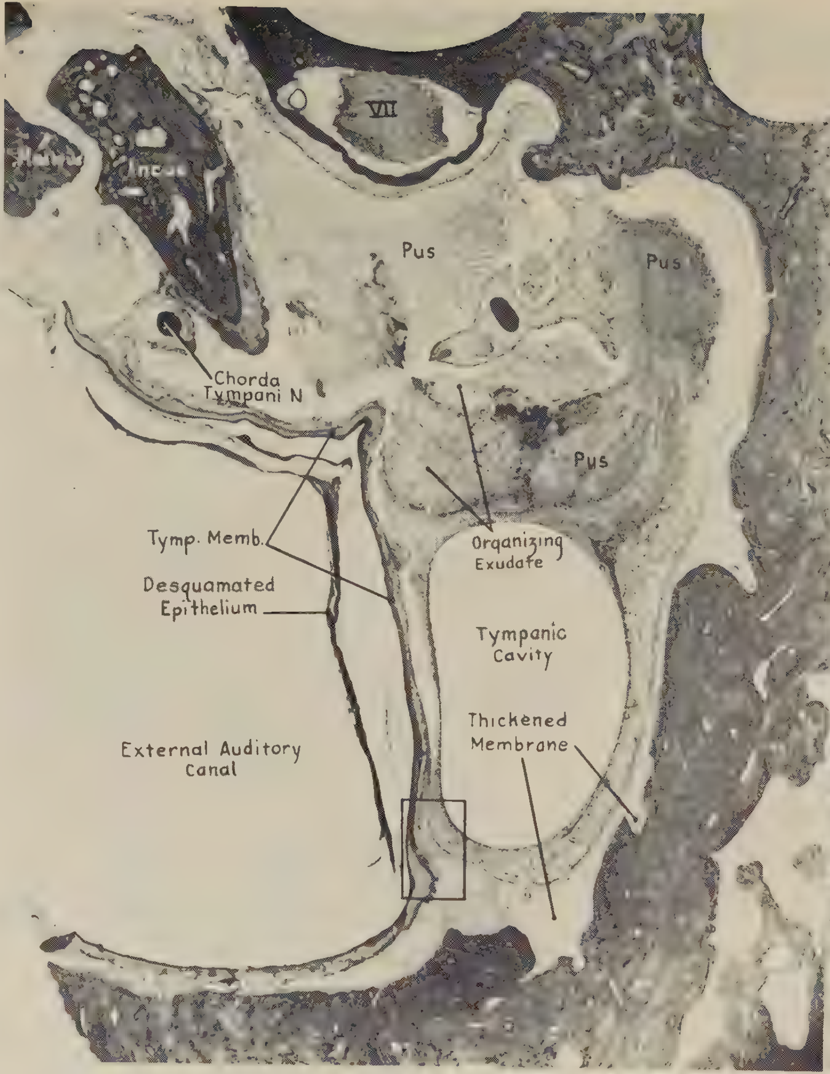
PERSISTENT MESENCHYME


Middle Cranial Fossa
M
I
Malleo-Incudal Articulation
Persistent Mesenchyme
S. C.
Subarcuate . Fossa
S. C.

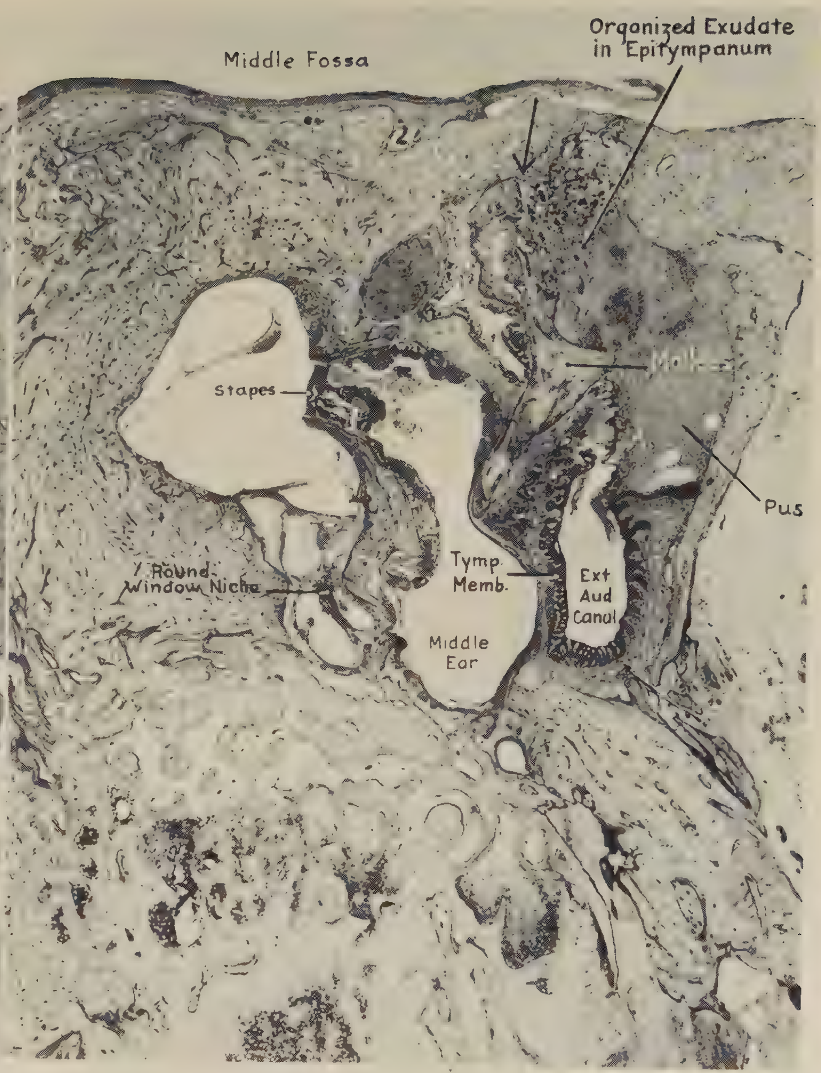
Primary mesenchyme in subarcuate fossa and persisting in middle ear. Horizontal section, approximately at level of attic of temporal bone, from newborn infant. The effect on function of the persistent tissue is obvious. (E. P. Fowler, Jr.)


External Auditory Canal
Tymp. Memb.
Incus
Pus
Malleus
Polypoid Inflammatory Thickening of Mucosa
Tensor Tympani M.
Stapes (Footplate)
Vestibule
Cochlea

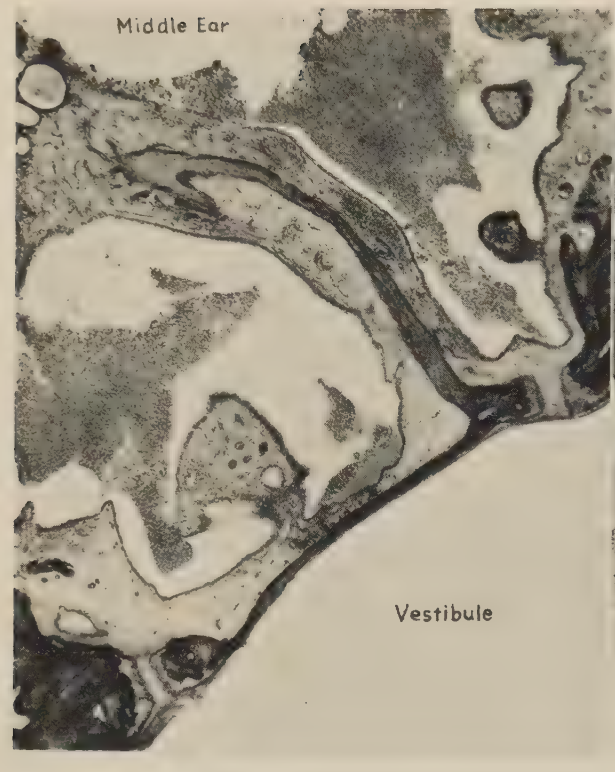
Purulent otitis media in a 7 month old infant. Horizontal section, approximately at level of upper edge of oval window. Entire middle ear is filled with pus. Note the polypoid thickening over promontory. x 15. (S. Guild)


VII
Incus
Pus
Pus
Chorda Tympani N
Pus
Tymp. Memb.
Organizing Exudate
Desquamated Epithelium
Tympanic Cavity
Thickened Membrane
External Auditory Canal

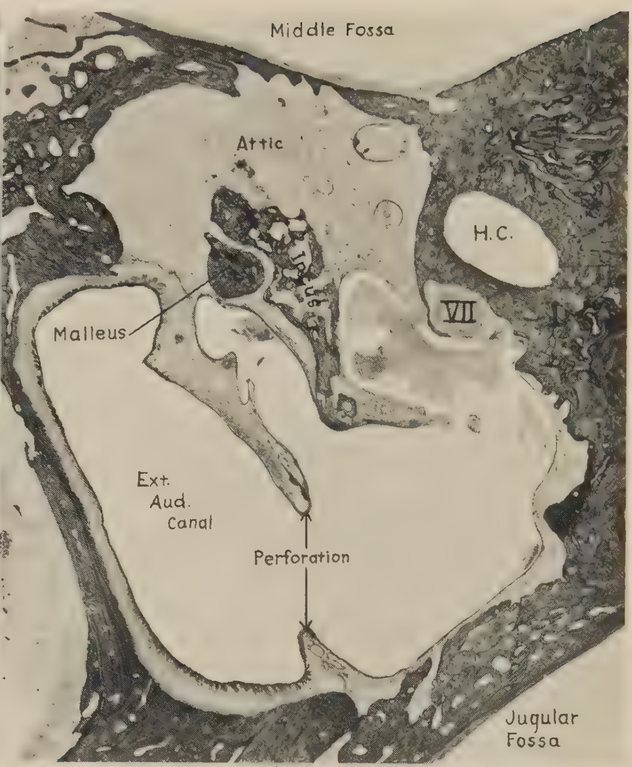
Otitis media, active subacute purulent. Vertical section. Mucosa of middle ear is greatly thickened. Ossicles are embedded in purulent exudate undergoing organization. x 13. (H. Semenov)


Middle Fossa
Organized Exudate in Epitympanum
Stapes
Pus
Round Window Niche
Tymp. Memb.
Ext Aud Canal
Middle Ear

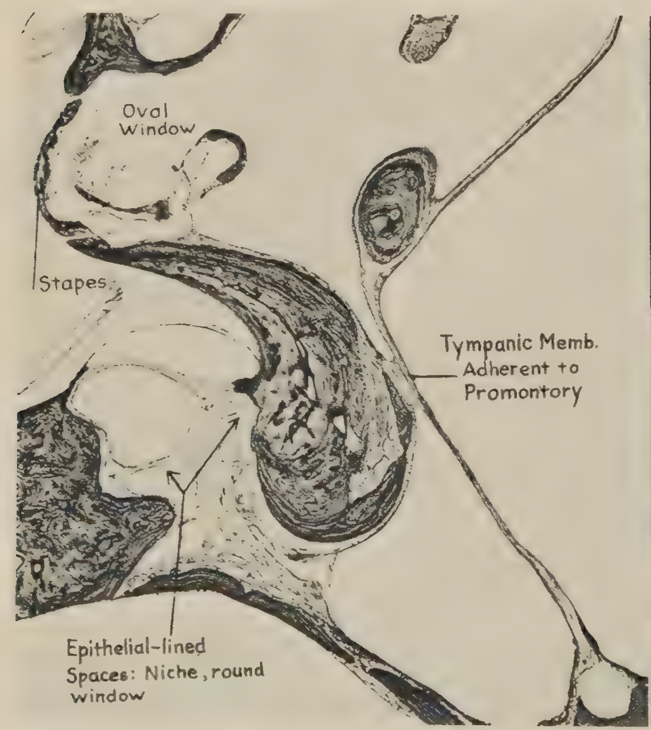
Otitis media, chronic, of 20 years' standing. Tympanic membrane very thick; middle ear epidermidalized (note rete pegs at bottom); organized exudate in epitympanum has frozen the malleus. Cholesteatoma (not included) had developed. Death from meningitis. (E. P. Fowler, Jr.)


Middle Ear
Vestibule

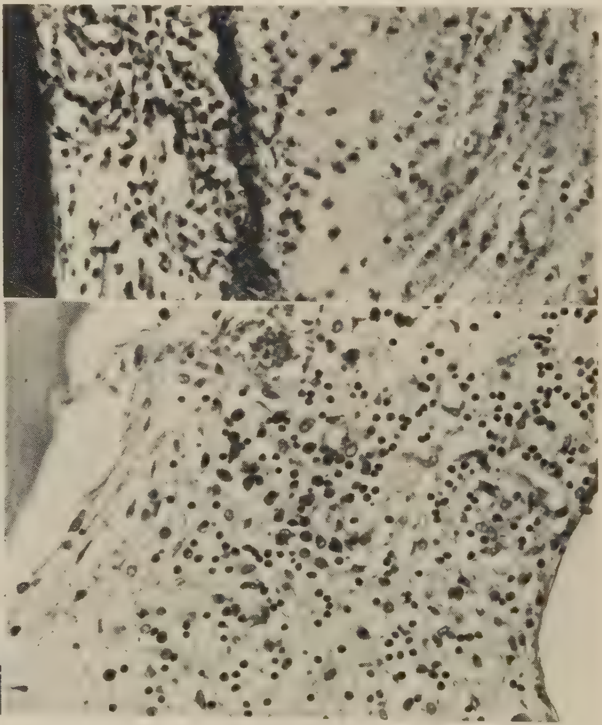
Otitis media, acute, purulent. Section includes oval window and stapes. All the mucosa is greatly thickened; purulent exudate fills the middle ear. (E. P. Fowler, Jr.)


Middle Fossa
Attic
H.C.
Incus
VII
Malleus
Ext. Aud. Canal
Perforation
Jugular Fossa

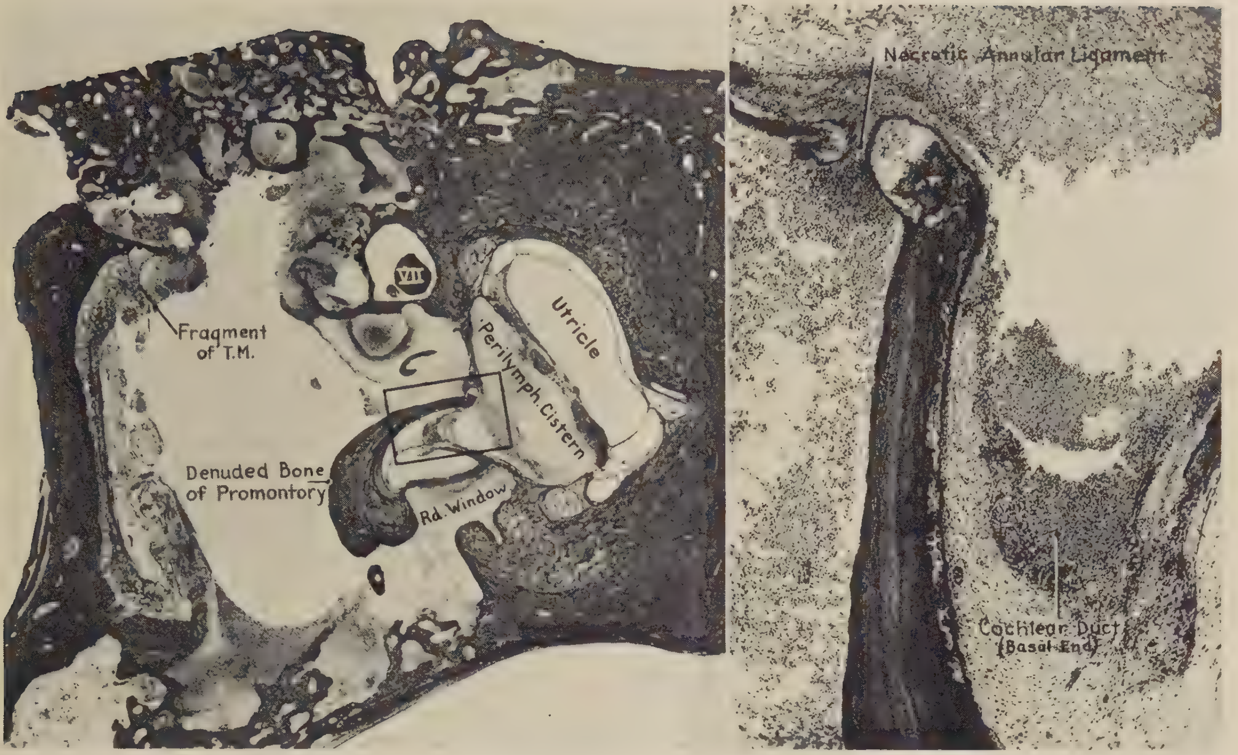
Otitis media, chronic. There is an old epithelized perforation of tympanic membrane; the attic is filled with granulation tissue, ankylosing the malleus and incus. x 6. (S. R. Guild.)


Oval Window
Stapes
Tympanic Memb. Adherent to Promontory
Epithelial-lined Spaces: Niche, round window

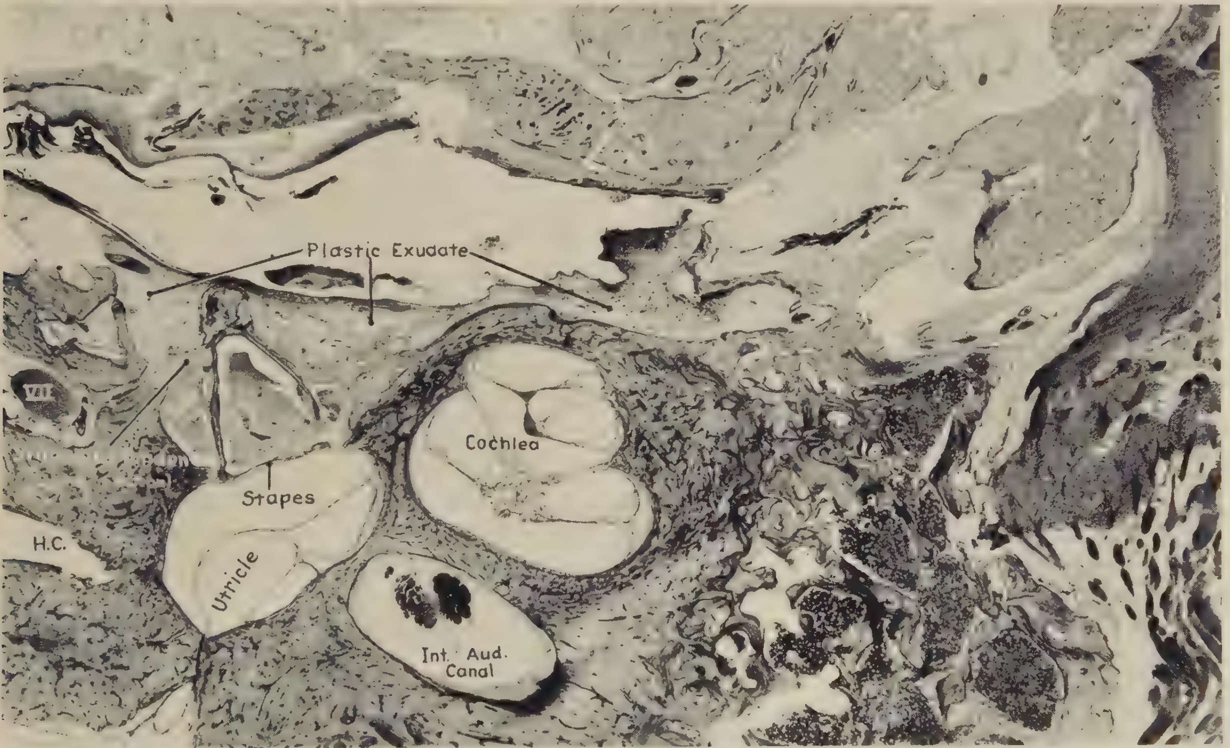
Residues of otitis media are adhesion of tympanic membrane to promontory and granulation tissue and epithelized spaces filling niche for round window. Hearing was not impaired. (S. R. Guild.)



Details of mucosal reaction in otitis media. A. From epitympanum—exudate in, and purulent exudate on the mucosa. B. From middle ear, two months' duration. Greatly thickened by edema and exudate, mostly mononuclear cells. Bony wall to left.


Fragment of T.M.
VII
Utricle
Perilymph. Cistern
Denuded Bone of Promontory
Rd. Window
Necrotic Annular Ligament
Cochlear Duct (Basal End)

Tuberculous otitis media, in adult with advanced pulmonary tuberculosis. Shortly before death, painless discharge from ear, positive for *M. tuberculosis*. Tympanic membrane largely destroyed. At left, necrotizing type with denudation of promontory, thick exudate in windows, purulent exudate in labyrinth. x 6. At right, rim of oval window and annular ligament necrotic; cochlear duct contains thick exudate. x 43. (S. Guild.)


Plastic Exudate
VII
Stapes
Cochlea
H.C.
Utricle
Int. Aud. Canal

Old healed tuberculous otitis media. Horizontal section. Organized exudate fills niches and immobilizes stapes and is adherent to walls of middle ear. No evidence of activity. Labyrinth uninvolved. (E. P. Fowler, Jr.)

CHAPTER 34

MASTOID AND MASTOIDITIS

The mastoid antrum is lined by a thin mucous membrane. In infants the osseous cortex is extremely thin and the petro-squamous suture is open, which explain the frequency of subperiosteal abscesses in early childhood. The development of the mastoid process coincides with the period during which the infant tries to carry or balance its head; by the age of two years the osseous formation is well established, trabeculae and a cellular system are present at six, and growth is completed at puberty.

The mastoid antrum is the posterior enlargement of the aditus. It has long been known that in the newborn this cavity has reached its full size. The mastoid cells communicate with the antrum and develop from it by a complicated process of bone absorption and new formation of trabeculae. As a rule, the new bone reduces the size of the antrum, and normally the adult antrum is smaller than in childhood. This rearrangement in the region of the antrum is difficult to explain. It is possible that development of the mastoid process follows Wolff's law in the formation of trabeculae.

The thinnest part of the mastoid region and the portion which has the most dehiscences is the roof. The subantral cells are small and the bony trabeculae thick. In the tip of the mastoid process the cells are usually large.

The aditus ad antrum in vertical sections is triangular in form and, when seen in the gross specimen, roughly resembles a prism. The upper portion is the bony tegmen, which in the middle ear portion of the aditus is designated as the tegmen tympani, and in the antrum, as the tegmen antri. The short process of the incus is anchored in the lower angle of the prism.

Pneumatization.—It is safe to say that the temporal bones of no two individuals show precisely the same distribution of pneumatization. But there are certain general patterns that it is well to know because of their importance in the dissemination of infections. Pneumatization may occur in any or all portions of the petrous bone in addition to the mastoid. The air cells may appear in the hypotympanum in close association with the middle ear and the eustachian tube; they may lie behind the bony labyrinth or may completely surround it. Not only does distribution of the air cells vary but also their size. The apex of the mastoid, for example, may contain either enormous cells or none, and if the bone does not become pneumatized, mastoiditis cannot develop. Beyond a few cells over the tubal apex, the petrosa usually is not pneumatized, but in three to four per cent of individuals pneumatization is extensive and includes the apex of the petrous pyramid.

In a roentgenologic study of both temporal bones in a group of 1524 men 20-21 years of age, predominantly without otic disease, Seppälä noted extensive pneumatization in 3.1 per cent, what might be termed normal or only slightly arrested pneumatization in 72 per cent, strongly arrested pneumatization in 14.9 per cent, and no development of air cells in 10 per cent. In 20 per cent, pneumatization was asymmetrical. He also reviewed material from 711 cases in which surgery on temporal bones had been performed. The incidence of mastoiditis was highest in very extensively but irregularly pneumatized bone and lowest in wholly compact temporal bones. The more serious intracranial complications were more frequent in association with strongly or completely arrested pneumatization.

Pathologic Pneumatization.—It is doubtful, from evidence presented thus far, whether the mild forms of infantile otitis media can actually arrest pneumatization. On the other hand, there can be no question but that suppuration which extends down to and includes the periosteum gives rise to sclerosis of the bone. Foreign body otitis media probably predisposes the membrane to secondary infection. It is possible, however, for this type of inflammation to create considerable hyperplasia of the mucous membrane. Ojala has recently reviewed the leading theories of pathologic pneumatization in connection with a histologic study of temporal bones from aged individuals and newborn infants.

Acute Mastoiditis.—Because of the free communication between the middle ear and the mastoid cells through the aditus, there is always a certain amount of mucosal inflammation in the mastoid in every case of infectious otitis media. When the infection results in bone involvement the mastoiditis becomes clinically evident. It is not necessary to review this evidence.

The reaction in the mucosa of the cells of the pneumatized portion of the mastoid is exactly the same as that of the middle ear. It consists of swelling from edema and congestion and from the accumulation of exudate, predominantly lymphocytes and plasma cells. The lumens of the air cells are narrowed or obliterated by the mucosal swelling and the accumulation of free exudate. The mucosa may be destroyed, and then it can be difficult to distinguish the air cell from an infected marrow space. The infection is spread primarily by continuity of structure through the communicating air cells. If the infection reaches the bone marrow, either directly by necrosis of the bony walls of the air cells, or along the perforating vessels of the lining mucosa, the more serious complications of mastoiditis become possible from the destructive effect of the resulting osteomyelitis. Necrosis of bone trabeculae of the cancellous bone and of the walls of the air spaces results in a localized collection of purulent exudate, the clinical empyema of the mastoid. If the necrotizing process extends through the cortical plates of the bone, the consequences are multiplied. When it erodes through the external plate, the pus burrows under the periosteum and produces a bulging abscess in back of the ear. If the erosion is through the tip of the mastoid, a deep cervical Bezold's abscess and cellulitis develop. When the osteomyelitis involves the inner tables of the mastoid the escape of pus will be beneath the dural periosteum, with development of epidural or perisinus abscess.

Another possibility is the extension of the infection into the zygomatic arch, causing osteomyelitis of that bone. Infection which gains access to the apical portion of the temporal bone usually passes through the more remote air cells, and unless drainage is effected, necrosive petrositis results.

In fulminant infections of the mastoid the reaction may include a large hemorrhagic component. This results from necrosis of the vascular walls by bacterial toxins, liberating varying quantities of blood into the mucosa and lumens of the air spaces.

When **chronic mastoiditis** develops in a poorly pneumatized temporal bone there is necrosis, then osteogenesis, and more and more thickening of the bone trabeculae. As a result the cortex, particularly, becomes ivory-like in consistency. This process is eburnation and it complicates operative procedures on the mastoid. The marrow spaces in the cancellous portions of the bone are largely obliterated by fibrous tissue which is obviously osteogenic, because the cells next to the old bone lamellae are lining up and producing layers of osteoid. At the same time in some areas there is continuing necrosis of bone lacunar formation by osteoclasts. It is unlikely that such a chronic process would be confined to the mastoid; more probably it would be part of osteomyelitic involvement of the middle ear. The cause of the so-called sclerotic mastoid is still to be clarified. Some subscribe to the theory that it is always due to an infectious process; others, that it is primarily developmental, and still others, that both factors may be involved. There is no doubt, however, that chronic otitis media and cholesteatoma are very rarely found in well pneumatized temporal bones.

Cholesteatoma (Pearly Tumor).—Cholesteatoma, in most instances, is the result of marginal perforation of the tympanic membrane and chronic inflammation of the middle ear and the mastoid antrum. The commonest site is the upper part of the middle ear, followed by the mastoid antrum and the mastoid and rarely by the petrous itself. It is more often seen in early adult life and often is preceded by a history of otitis media with scarlet fever in childhood.

In 11 cases of cholesteatoma received at the Army Institute of Pathology during the war, symptoms of chronic otitis media had been present from 8 months to more than 40 years before operation. At autopsy, in three of these there was sinus thrombosis associated with brain abscess: epidural abscess in one, acute meningitis in another, and abscess around the lateral sinus in the third.

Begley, McDonald and Williams have recently reviewed the significant literature dealing with the histopathology of cholesteatoma in a study designed to prove the epidermic nature of the lesion. A lively critique of the theories of pathogenesis previously offered and an excellent illustrative coverage of the lesion can be found in an article by Tumarkin, although the thesis he advanced is controversial.

The formation of cholesteatomas of the middle ear depends on alteration to the squamous type of the epithelium lining these cavities. If it is localized to portions of the middle ear, as described under otitis media, the epidermization always is due to re-epithelization of the middle ear by the extension of the squamous epithelium of the external auditory canal through a marginal perforation in the tympanic membrane. Wherever the squamous epithelium is present in the cavities there is a constant and persistent accumulation of exfoliated keratin and a certain amount of exudate. It is the keratin that is responsible for the subsequent damage. The large amount of cholesterol often present in the contents comes from the fatty components of the desquamated epithelial debris. The accumulation of this debris causes an increasing pressure on the bony walls of the involved cavity. As is usual under these circumstances, the bone undergoes pressure atrophy, with eventual formation of a large, radiologically demonstrable cavity. Cholesteatomas developing in the middle ear may become evident through bulging of the contents through the tympanic membrane. If there is no operative interference, erosions may include the entire thickness of the bone, and the cyst may erode the horizontal semicircular canal or emerge into the cranial cavity. Cranial invasion is particularly likely to result from cyst formation below the labyrinth and in the petrous pyramid. These are thought by many to be primarily epidermal cysts resulting from congenital inclusions of nests of squamous epithelium in the bone. Such a cholesteatoma is not primarily on an inflammatory basis and is comparable to the craniopharyngioma of the sphenoid. When only the middle ear is involved and there is drainage through the perforation of the tympanic membrane, the characteristic foul smelling discharge contains keratin flakes and cholesterol crystals.

The term cholesteatoma used in this instance is not correct in spite of the usual cholesterol content. Cruveillier, who first described the lesion in the early part of the 19th Century, called it the pearly tumor "tumeur perlée," and it might be wise to revive the term. Pathologically, the lesion is an epidermal inclusion cyst or a keratin cyst, but the term cholesteatoma is so well rooted in clinical nomenclature that the purist would have little success in attempting to change it.

Cholesteatomas have been divided into two classes: *secondary,* including the common variety just described, which is on an inflammatory basis, and the one that arises from invagination and subsequent isolation of Shrapnell's membrane, and *primary,* which results from the embryonal inclusion of squamous epithelium in the developing bones. The secondary cholesteatoma from Shrapnell's membrane occurs as the result of adhesions which extend from the external tympanic membrane to the medial wall of the middle ear. These adhesions isolate the attic and antrum which then become epithelized from the squamous epithelium of Shrapnell's membrane. From here the lesion may extend into the mastoid and petrous. The end results are the same as in the infectious secondary type, with the squamous epithelium growing through a marginal perforation.

Histologically, the cholesteatoma is lined by squamous epithelium that has a well defined basal layer which at times includes rete pegs. The thickness of the squamous layer varies greatly. In older lesions it is limited to one or two cells in thickness. It has a well marked, dark granular layer and overlying this are an abundance of keratin scales. Intact scales can be traced into the cyst space, but around the characteristic slits that mark the site of cholesterol crystals the contents of the cyst become more and more granular. Ordinarily there is no cellular content. The epithelium rests on a narrow zone of vascular connective tissue that may contain a few small mononuclear cells. This tissue is applied closely to the bone in which the normal air spaces may be obliterated, greatly reduced in size by granulation tissue, or filled with hyalinized material. The epithelium lining these air spaces is usually compressed. The bony trabeculae show very little osteoclastic absorption; the reduction in bone is by resorptive atrophy.

According to Wittmaack, chronic otitis media and cholesteatoma develop only in temporal bones that are poorly pneumatized because of otitic processes during infancy. The lack of air cells is an important anatomic factor in the etiology.

The lesion is difficult to eradicate, because any epithelium that remains in crevices and fissures after attempted removal of the cholesteatoma forms a nidus for the regrowth of the lesion.

Cholesteatoma-like lesions arising in the external auditory canal were mentioned in Chapter 35. For further discussion of the subject the reader is referred to the recent article by Altmann and Waltner.

GRANULOMATOUS INFLAMMATIONS MIDDLE EAR AND TEMPORAL BONE

Tuberculosis of the middle ear is rare, particularly in this country, but in "endemic centers" the incidence in infants and very young children is much higher than in older age groups. It may be a primary malignant infection of the bovine type in infants, but in older individuals it is usually secondary to active pulmonary disease. In infants the infection reaches the middle ear through the eustachian tube by regurgitation, by direct extension from a tuberculous lesion in the nasopharynx, or most commonly, by the blood stream. In the last instance, the primary focus is not necessarily in the lungs, but in less obvious situations such as the bones. As a complication of pulmonary tuberculosis the transmission is usually hematogenous. This is the predominant pathogenesis in this country. It has been Fowler's experience with adults that frequently a history of operation on the lung on the *opposite* side precedes by several months the tuberculous process in the ear. The course of the disease is largely dependent on the degree of the patient's immunity. As a primary infection in infants who have not as yet developed an immunity, and in the young adult suffering from hematogenous dissemination, the process may be progressively destructive by caseation and by very active tuberculous osteomyelitis of the affected bone or necrosis of the soft parts. Death is hastened by secondary pulmonary infection. Blood-borne infections commonly involve primarily the cancellous portions of the temporal bone rather than the mucosa, which is principally affected when the bacilli reach the middle ear through the eustachian tube. The frequency of facial paralysis is evidence of the incidence of bone involvement. Another occasional serious complication is erosion into the carotid canal, leading to hemorrhage or to thrombosis of the carotid artery. Infection may spread to the labyrinth, usually by way of the oval or round window.

The infection usually results in extensive necrosis of the bone, at times with formation of large sequestra, the activity intensified by secondary bacterial infection. In very active cases the tubercles, miliary and conglomerate, are readily recognized under the microscope and tubercle bacilli can be demonstrated. The disease is sometimes of a more sluggish fibroid character, with fibrous replacement of the mucosa and an exudative component more prominent than active tubercles. This form is more commonly found in the bone. The external tympanic membrane is always involved eventually, with the formation of tubercles resulting in fixation of the membrane and multiple perforations which quickly coalesce into a large perforation.

The preauricular lymph node is practically always involved. If tubercle bacilli cannot be demonstrated in the discharge from the infected ear, this node will usually show typical tubercles as a diagnostic criterion.

The mastoid is occasionally the seat of active tuberculous osteomyelitis. Such a case is illustrated in the following plates. The curettings of a mastoid are from a three-year-old boy who had had unilateral otorrhea and otalgia for 18 months. The mastoid was very tender, and the external canal was filled with foul-smelling, purulent discharge. An x-ray of the mastoid showed complete absence of cell structure with a central loss of trabeculation; on operation this portion was found to be a mass of granulation tissue and thick exudate.

The infection reaches the mastoid and petrous portion of the temporal bone either by spread from the middle ear through the aditus ad antrum or through the blood stream.

Syphilis.—The cartilage of the external ear is affected in the tertiary stage by destructive gummatous lesions. Involvement of the middle ear and temporal bone is also usually gummatous. The mucosa of the middle ear is occasionally the site of secondary lesions that produce a MIDDLE-EAR DEAFNESS, a contradiction to the belief that syphilis results only in nerve deafness. Goodhill, in a study of material from 16 cases of syphilis of the inner ear, found various deformities of the bony semicircular canals and atrophy of the neural epithelium of the cochlea and vestibule. Endarteritis is more prominent in the acquired infections. Cerebrospinal involvement in acquired syphilis is a well known cause of deafness.

The ear and temporal bone are also affected by congenital syphilis in the form of an active gummatous reaction which destroys all of the structures involved. Localizing primarily in the bone, it causes destruction of the cancellous portion of the bony capsule of the labyrinth, the mastoid, or portions of the petrous. Residua of an active phase, such as scarring, will involve the ossicles and possibly obliterate the semicircular canals. When periostitis develops in the bony labyrinth, the perilymphatic spaces are compromised or obliterated. When the infection has occurred early in intrauterine life, there may be grave interference with the normal development of the bony and membranous elements of the middle and inner ear and atrophy of the neural elements of the membranous labyrinth. Nerve deafness from congenital syphilis may not become manifest until the tenth to twelfth year. In fact, in the cases studied by Mayer and Fraser, the effects became evident in apparently healthy individuals who were as much as 20 years of age. The pathologic changes were chiefly gummatous involvement of the spongy bone with extension to the bony and membranous labyrinths. This primary destruction and the secondary scarring lead to narrowing or obliteration of the canals, hydrops of the ducts, ankylosis of the ossicles, and nerve damage. Collateral evidence of congenital syphilis is of help in the diagnosis of the otic manifestations. This includes interstitial keratitis, Hutchinson's teeth, residua of syphilitic involvement of bones and soft tissues elsewhere.

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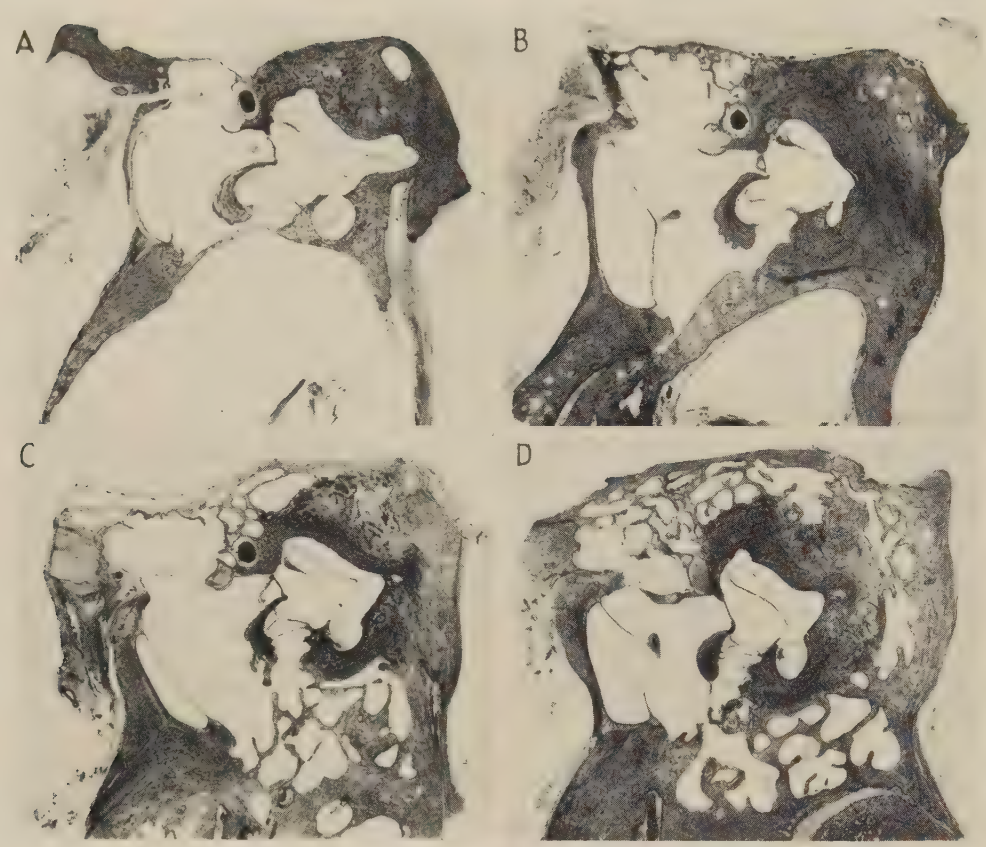
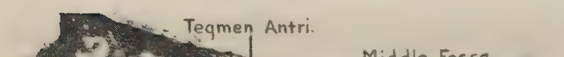
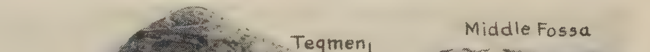
VARIATIONS



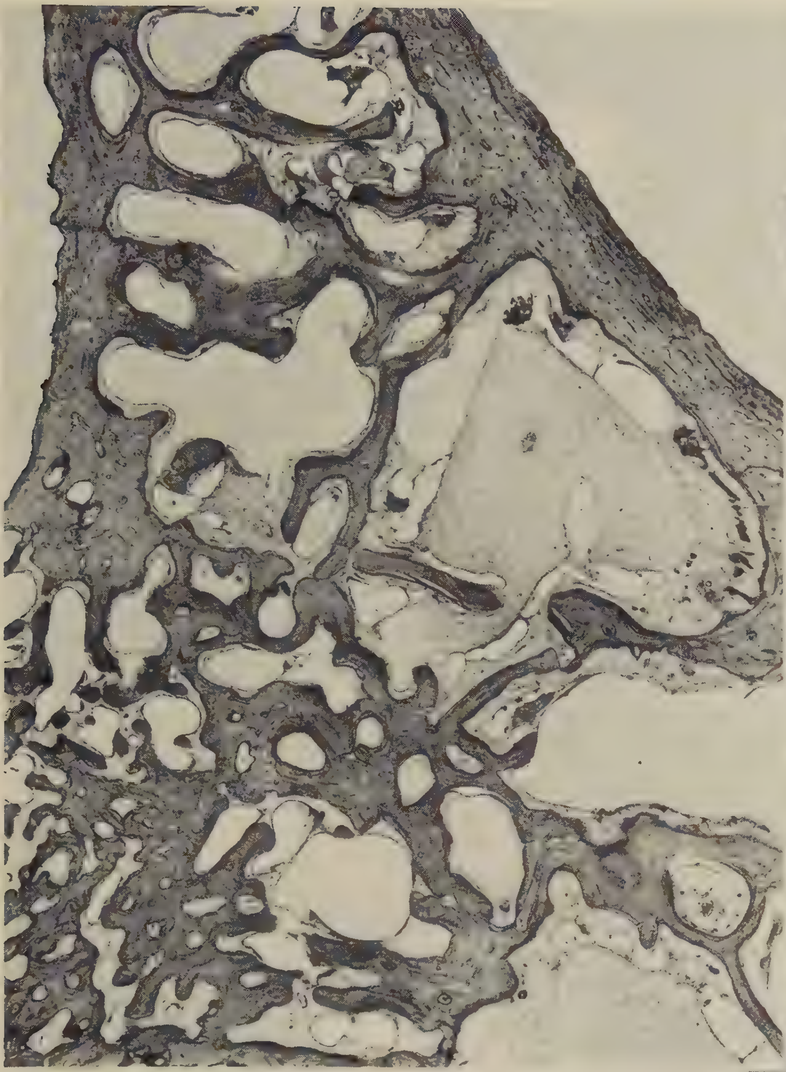
Normal variations in extent of perilabyrinthine pneumatization. A. None. B. Practically none, some of petrous ridge. C. Hypotympanic. D. Extensive. (S. Guild.)


Tegmen Antri.
Middle Fossa
Mastoid Antrum
Ext. Aud. Canal
Post. Fossa
×
×
×
×

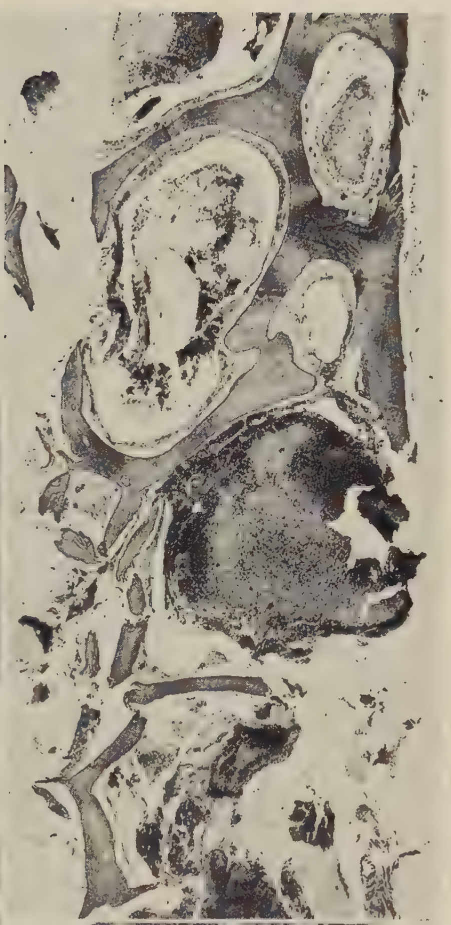

Tegmen
Middle Fossa
H.C.
P.C.
H.C.
Shrapnell's Memb.
Middle Ear
P.C.
Tymp. M.
Posterior Fossa
Jugular Bulb
Sigmoid Sinus

Sclerotic mastoid, no air cells but red-marrow-containing spaces. Note delicate tegmen. (E. P. Fowler, Jr.)

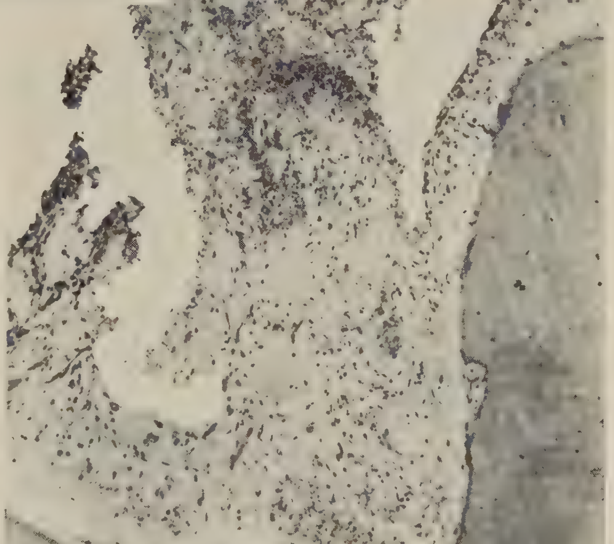
Total absence of perilabyrinthine pneumatization. The tegmen here is almost free of bone. Note extreme retraction of Shrapnell's membrane. H.C., P.C.—Horizontal and posterior semicircular canals. (E. P. Fowler, Jr.)



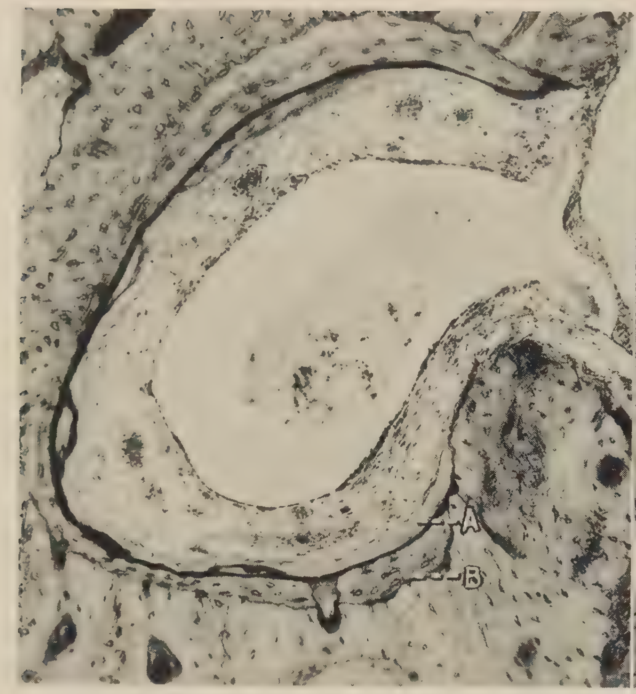
Mastoiditis, left, mild *(above),* in an adult, with no roentgenographic evidence of left mastoid involvement. Otitis media one month before death followed by acute mastoiditis on right. Edematous, thickened, focally congested mucosa; cuboidal and columnar epithelium; air cells contain some fluid and cellular exudate and edematous granulation tissue that resembles persistent mesenchyme. (E.P. Fowler, Jr.)



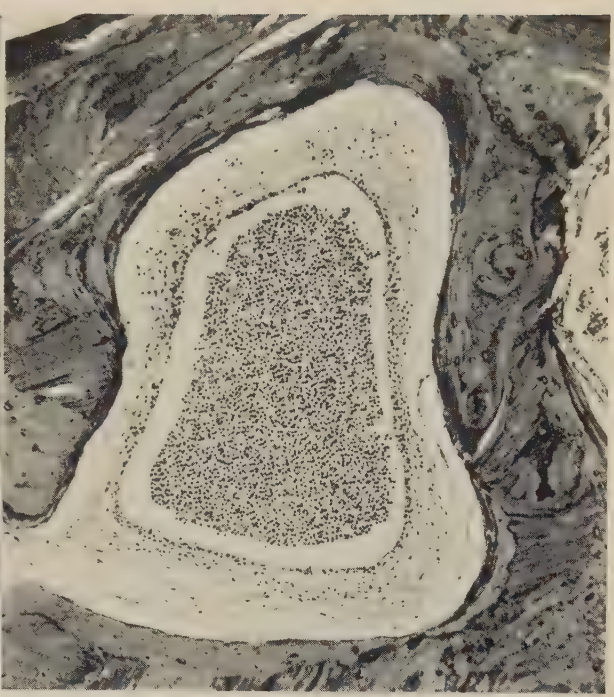
Acute mastoiditis, hemorrhagic *(upper right).* Probable cause, *Streptococcus hemolyticus.* All cells filled with purulent hemorrhagic exudate. x15. Otalgia developed in a man who had no previous cold; deafness with intense pain and tinnitus eighteen hours later. Bloody serum escaped on incision of bulging drum. Mastoidectomy performed on seventh day; air cells found filled with bloody exudate. Uneventful recovery. (S.S. Hall, Clarksburg, W.Va.)



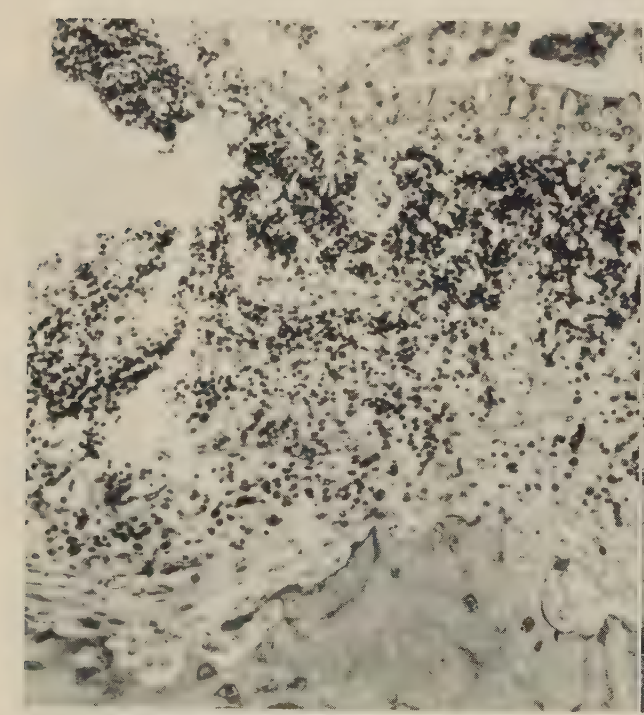
Thickened, congested mucosa of mastoid cell *(lower right)* of same patient contains focal hemorrhages and inflammatory cells. Hemorrhagic exudate adheres to surface, devoid of epithelium. Note early penetration of exudate by mucosal fibroblasts. x120.



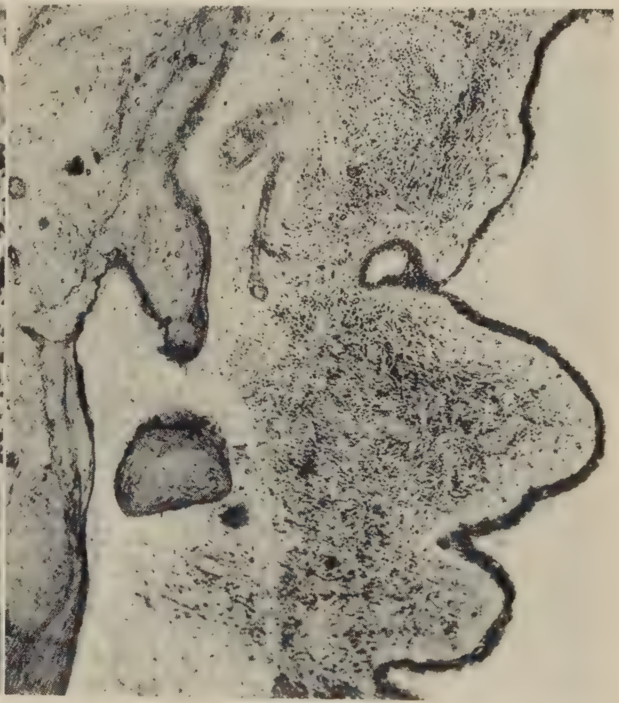
Mastoiditis, early recurrent infection. Seropurulent exudate. Recently formed osteoid **(A)** and layer of bone **(B)** laid down in response to previous infection show how repeated infection may fill cell with new bone. Case of recurrent low grade otitis media; mastoid clinically negative. (E.P. Fowler, Jr.)



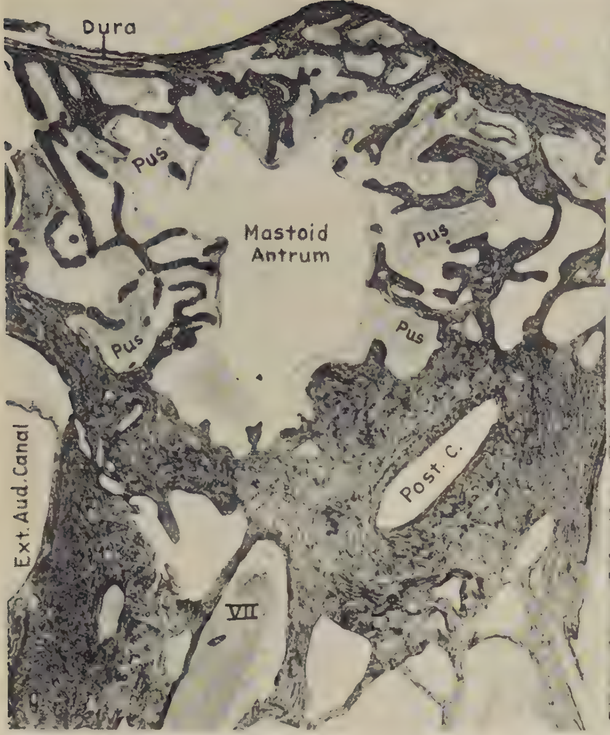
Acute suppurative mastoiditis. An air cell is filled with purulent exudate. Its thickened mucosa is edematous; is diffusely infiltrated by polymorphonuclear leukocytes; and is lined by a single layer of cuboidal epithelial cells. Numerous dilated capillary vessels. x75.



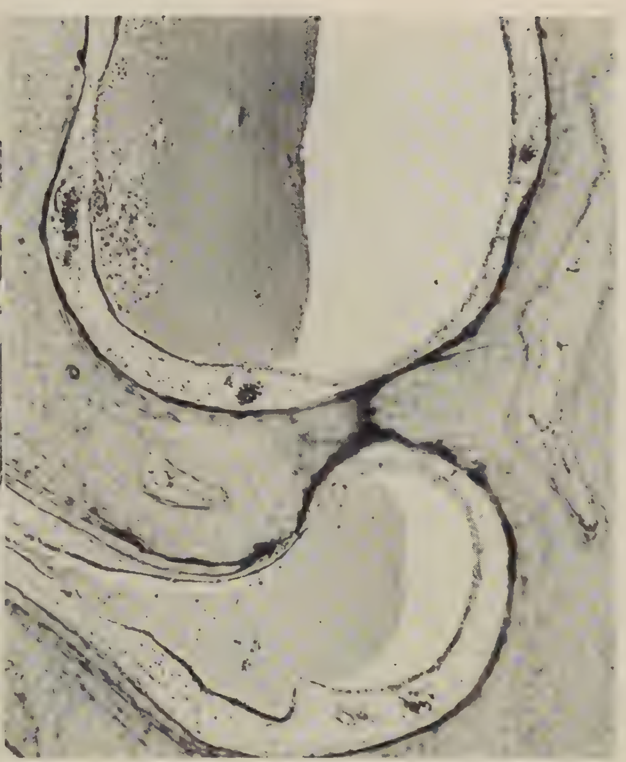
Chronic suppurative mastoiditis, from 7 year old boy with otalgia for four weeks, then purulent otorrhea, and death from streptococcic meningitis. Dense inflammatory exudate, chiefly lymphocytic; hyperplastic epithelium; osteoclastic resorption of bone. x150.



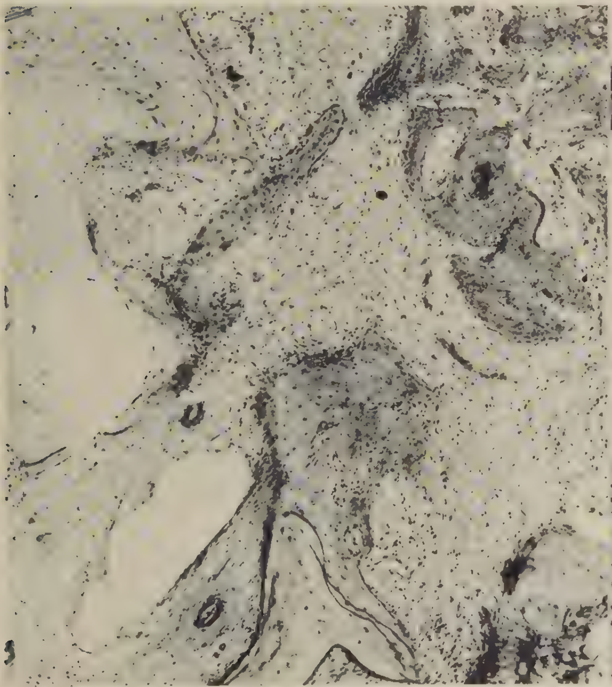
Chronic suppurative mastoiditis in patient who developed petrositis. The polypoid, congested mucosa shows evidence of edema and fibrosis and is heavily infiltrated by acute and chronic inflammatory cells. Prominent hyperplastic surface epithelium. x75.



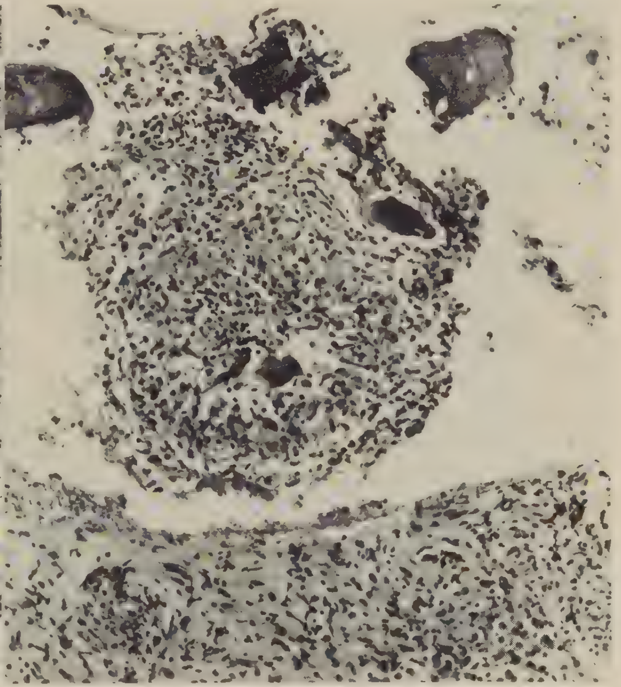
Early mastoid involvement, in an adult with acute suppurative otitis media (shown on a previous plate). Pus has invaded mastoid antrum and has extended into adjacent air cells. x5. (S.R. Guild.)



Catarrhal mastoiditis complicating early otitis media. Mucosa edematous; serous, almost acellular exudate in lumens; marked vascular congestion; high cuboidal epithelium. x70. (E.P. Fowler, Jr.)



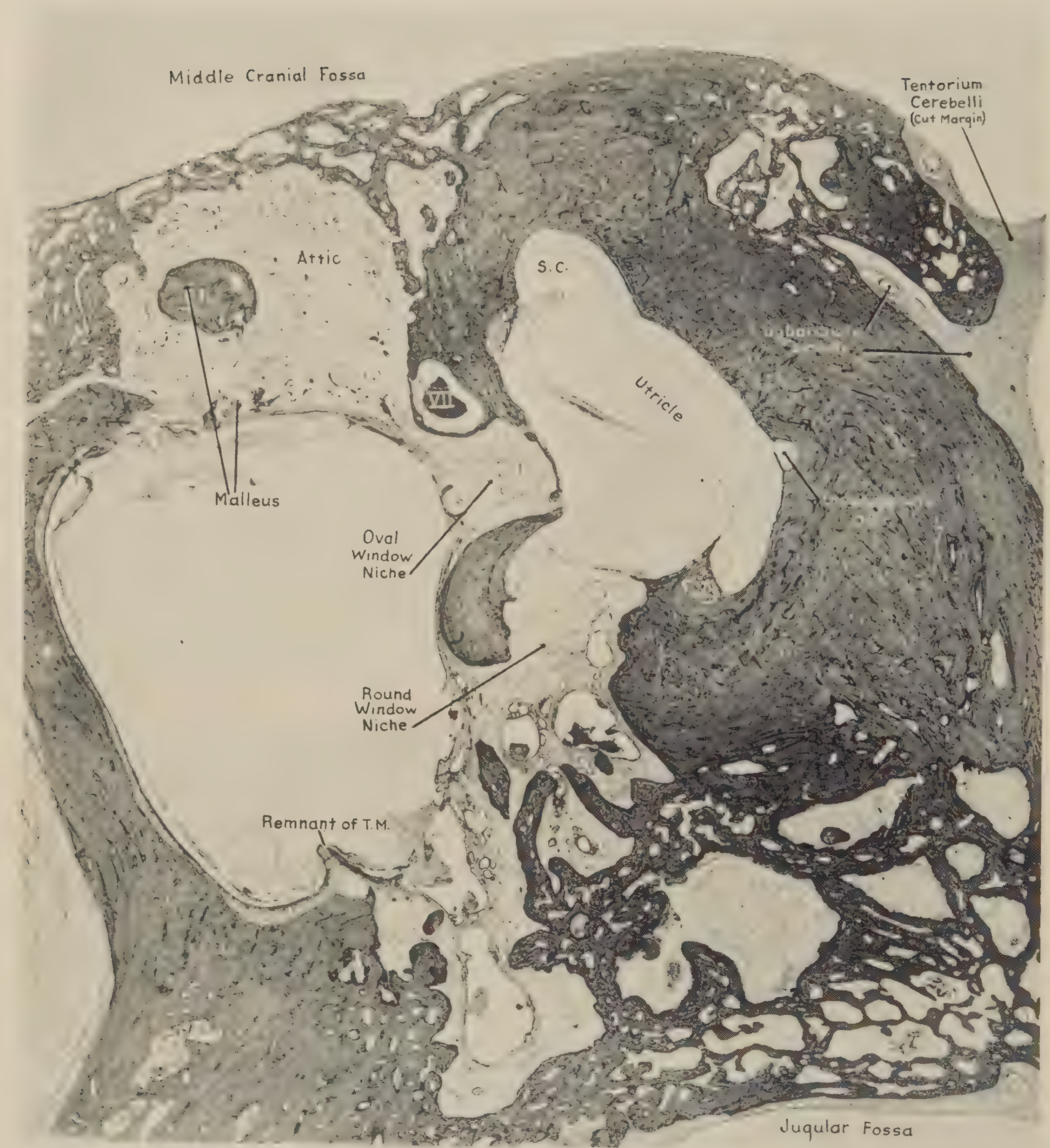
Chronic osteitis of mastoid, from a case of acute and chronic petrositis with intracranial extension of infection. Extensive fibrosis; irregular spicules of newly formed bone, some deposited on trabeculae of preexisting bone. x55. (E.P. Fowler, Jr.)



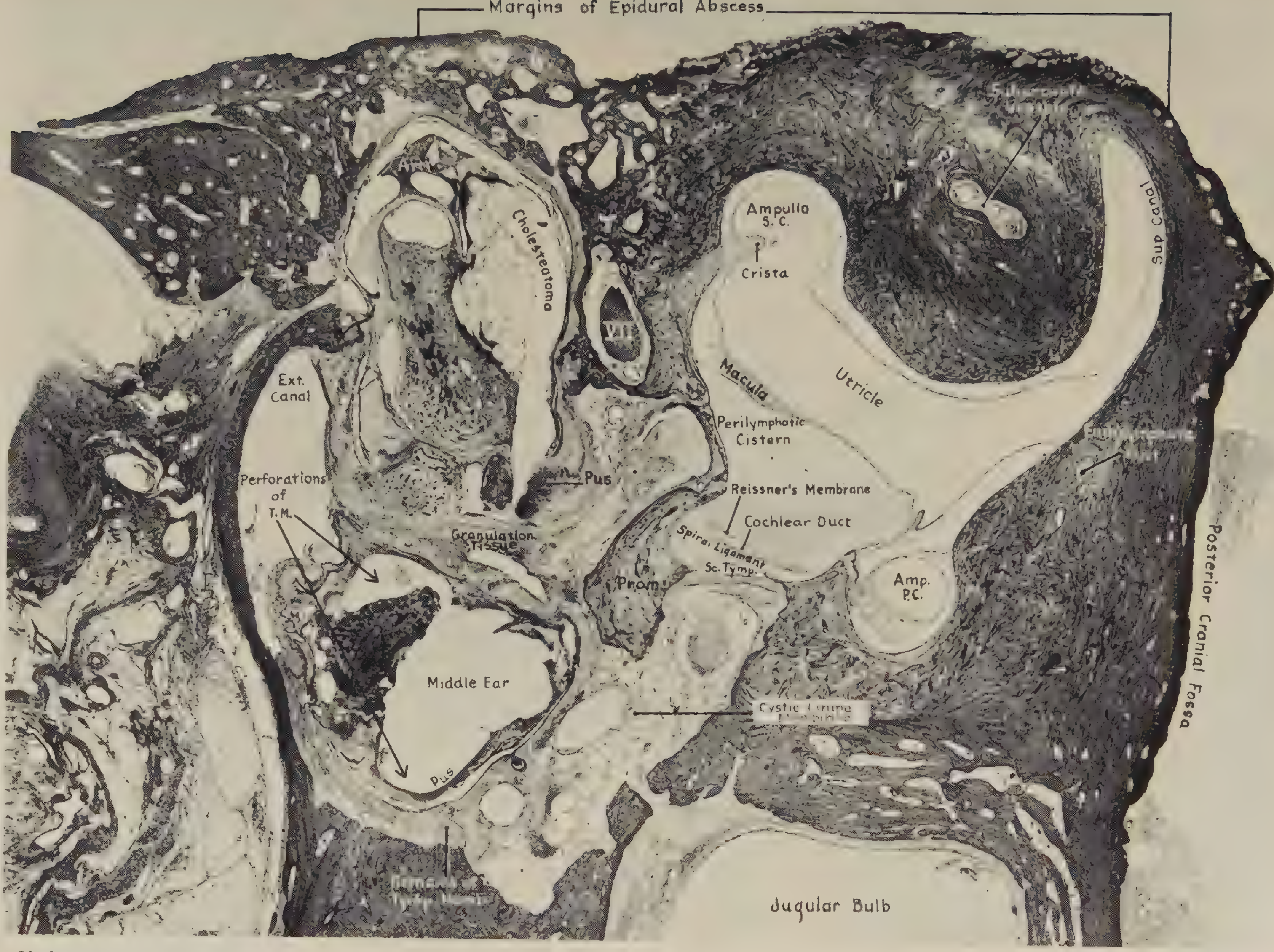
Tuberculous mastoiditis, from a 30 year old man with unilateral otorrhea for eighteen months. Tympanic membrane perforated; external canal filled with foul debris. Necrosis of bone; granulomatous inflammation, including typical tubercles. x135. (S.S. Hall, Clarksburg, W.Va.)

CHRONIC OTITIS MEDIA

EPIDERMIZATION OF MIDDLE EAR

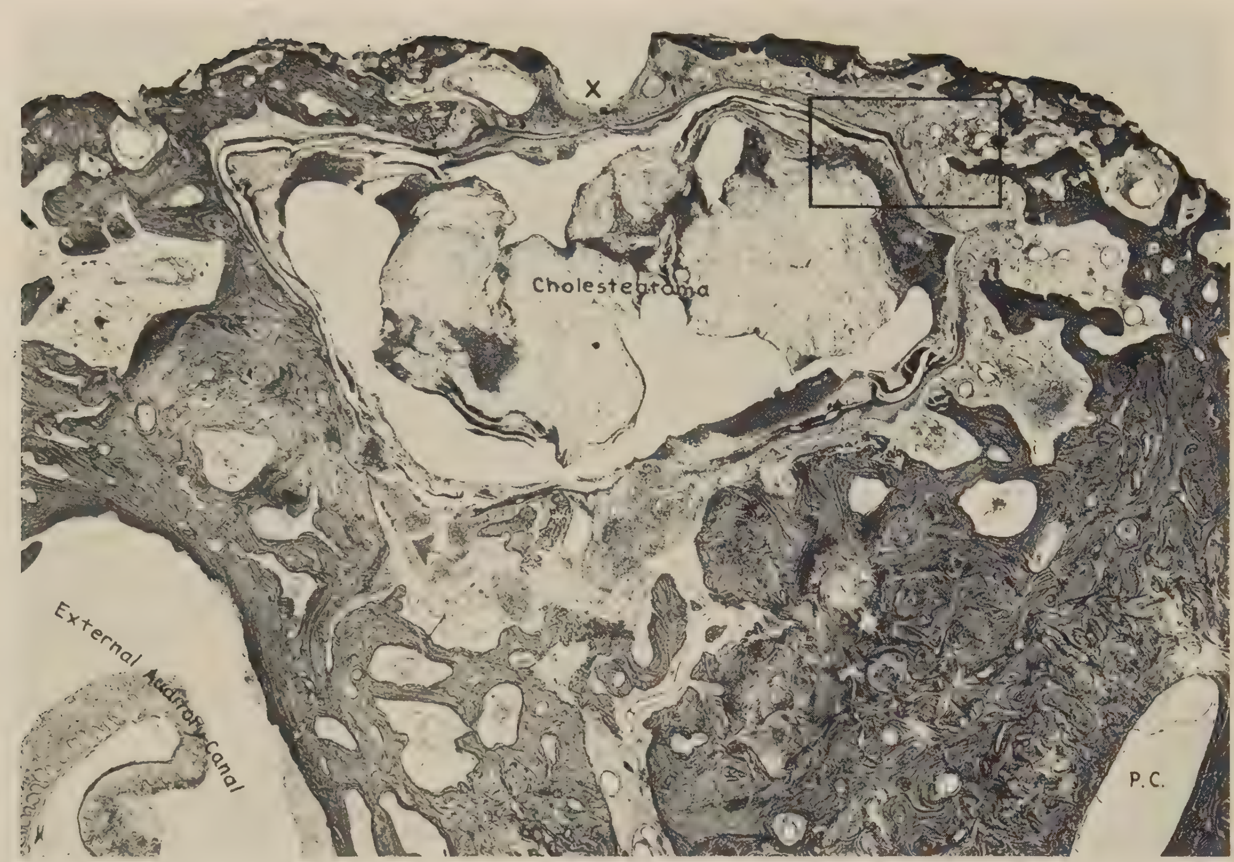

Middle Cranial Fossa
Tentorium Cerebelli (Cut Margin)
Attic
S.C.
VII
Utricle
Malleus
Oval Window Niche
Round Window Niche
Remnant of T.M.
Jugular Fossa

Vertical section through oval and round windows of the temporal bone of an adult with long-standing otitis media. Only a small remnant of the tympanic membrane is present and the ossicles have also been destroyed, except for the footplate of the stapes and a portion of the head of the malleus. The attic (epitympanic recess) and the niches of the oval and round windows are filled with loose fibrous tissue and granulation tissue, containing cyst like spaces of varying size, lined by flattened, cuboidal or columnar epithelium. Some of these spaces retain their connection with middle ear epithelium, which readily reepithelizes eroded surfaces, and epithelizes granulation tissue surfaces. Except for a part of its medial labyrinthine wall, the entire middle ear is lined by squamous epithelium, continuous with that of the external auditory canal. This epithelium is prevented from invading the attic by the granulation tissue filling it. (S.R. Guild.)

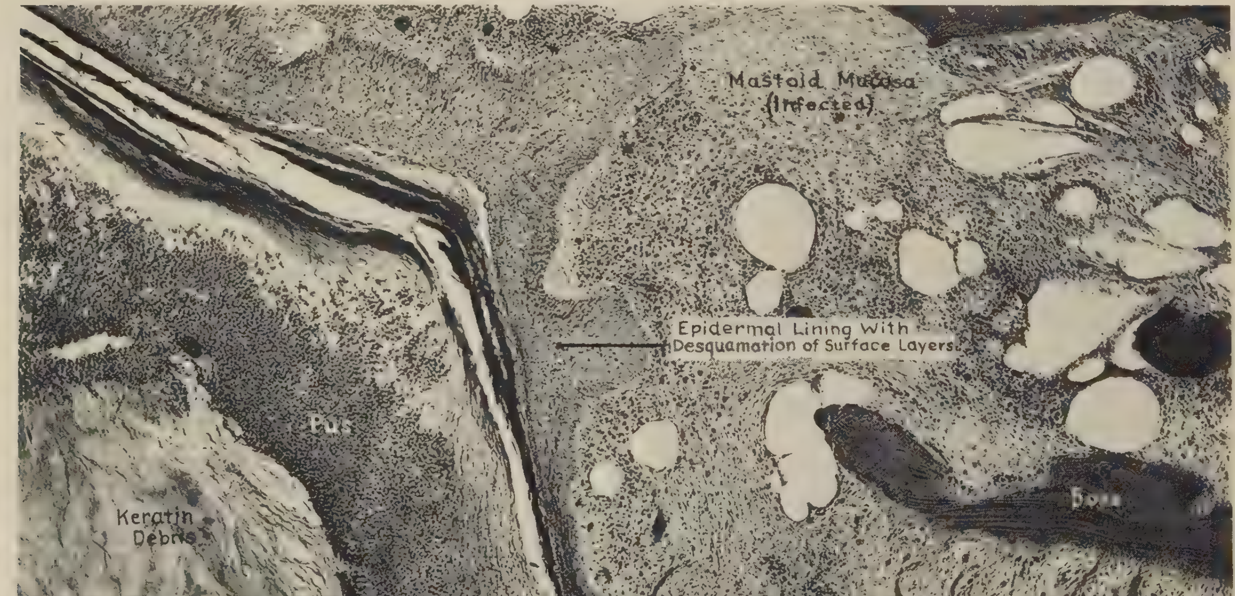

Margins of Epidural Abscess
Sup Canal
Posterior Cranial Fossa
Ampulla S.C.
Crista
Utricle
Macula
Perilymphatic Cistern
Reissner's Membrane
Cochlear Duct
Spiral Ligament
Sc. Tymp.
Amp. P.C.
Prom
Cholesteatoma
VII
Pus
Granulation Tissue
Ext. Canal
Perforations of T.M.
Middle Ear
Pus
Cystic Lining
Jugular Bulb

Cholesteatoma, epitympanic recess. Vertical section through oval and round windows; from a 16 year old boy who died of temporal lobe abscess, margins of which are indicated above. Discharge from ear, persistent since he had measles at the age of nine, and headaches in recent years. Evidences of severe chronic suppurative otitis media. Cholesteatoma cavity in attic in this plane is walled off by granulation tissue from squamous epithelial lining of middle ear space, which is continuous with the lining of the external canal. (S. Guild.)

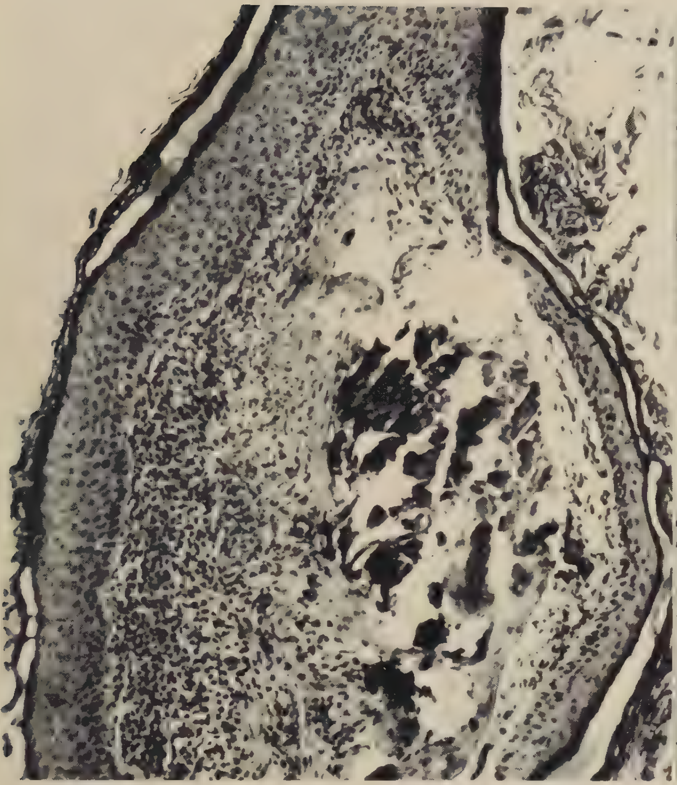
This section also affords a review of the relationship of the structures in this plane.


X
Cholesteatoma
External Auditory Canal
P.C.

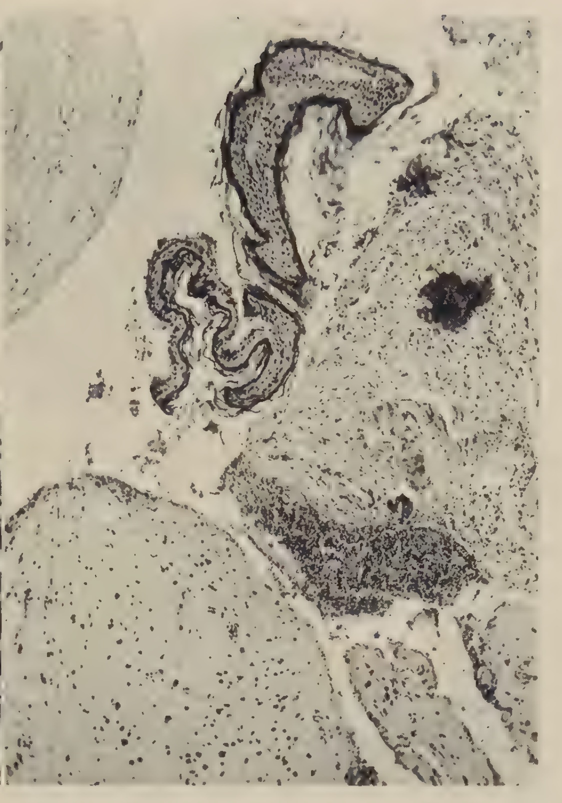
Cholesteatoma in mastoid antrum. (Same case as preceding plate.) The communicating spaces are filled with granulation tissue. Expansion of the mass with erosion of bone are attributable to the pressure exerted by accumulating keratin and cellular debris. **X,** area of erosion by cholesteatoma into cranial cavity. **P.C.,** posterior semicircular canal. x11. (S.R. Guild.)


Mastoid Mucosa (Infected)
Epidermal Lining With Desquamation of Surface Layers
Pus
Keratin Debris
Bone

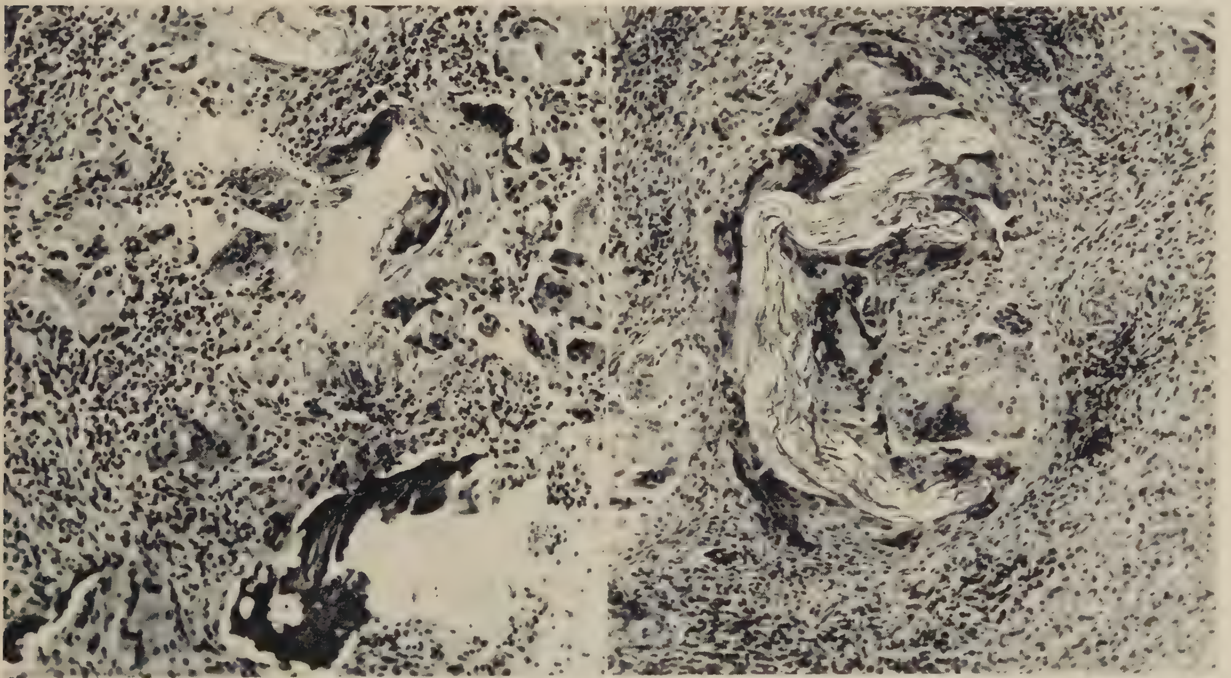
Magnification of blocked area above. Note large pegs of squamous epithelium. Bone trabeculae are undergoing bland and osteoclastic destruction. (S.R. Guild.)



Remnants of necrotic bone are surrounded by dense exudate and the epithelium of a cholesteatoma. The squamous epithelium shows normal, orderly maturation and is producing abundant keratin. Cholesteatoma, mastoid. x125.



Intracranial extension of a cholesteatoma that has eroded through bone into cranial cavity. The squamous epithelium lies adjacent to brain tissue. Destruction is by pressure of accumulating keratin. x90.



Foreign body granulomas may form about keratin and necrotic bone and are important diagnostic features when only small biopsies are obtained. *Left:* granulomatous reaction with numerous foreign body giant cells about strands of keratin and ragged bone spicules. From a mass presenting through the tympanic membrane. *Right:* foreign body granuloma about flaky keratin, in a mass of granulation tissue removed from tympanic membrane area. Both x125.

CHAPTER 35

TEMPORAL BONE

PETROUS PORTION OF TEMPORAL BONE

The lining of the petrosal air cells lacks nerves, glands, and secretory cells; it should, therefore, be spoken of as a rudimentary fibro-epithelial membrane, of obvious identity with the lining membrane of the mastoid air cells. In fact the pneumatic cells of the petrous pyramid are subject to exactly the same disorders as are those of the mastoid. In acute otitis media with pus formation, a certain amount of exudation will be seen in some of the petrosal cells; however, this does not always imply that suppuration is present. It is well known that the mastoid cells are involved in ordinary acute otitis media and that spontaneous resolution of the infection usually occurs. Experience has made it possible to distinguish between otitis media that will resolve spontaneously and that which calls for surgical intervention, and a similar situation obtains in petrositis.

Petrositis is a direct extension of middle-ear infection by continuity of structure through the communicating air cells. The distribution of the infection in this manner varies, of course, with the extent and location of pneumatization of the petrous pyramid. The reaction in these mucosa-lined spaces is the same as in the rest of the aerated cavities, but it is more serious because osteomyelitis develops either by direct extension of the infection into the surrounding bone through ulceration of the mucosa, or as the result of infectious thrombophlebitis extending from the mucosa into the cancellous portions of the bone. When osteomyelitis becomes established, erosion of the inner cortex of the bone is possible, with the development of subdural abscess or of purulent meningitis. When the erosion occurs near the sigmoid sinus, there is the further serious complication of thrombosis of the large venous sinuses at the base of the skull. Infection of the venous sinuses is possible also by the extension of septic thrombophlebitis of the contributing veins. Extension of infection through the apex of the petrous pyramid is, in rare instances, a cause of retropharyngeal abscess.

GRADENIGO'S SYNDROME. This is a clinical syndrome based on the spread of purulent infection of the middle ear to the tip of the petrous bone by way of the peritubal air spaces of the carotid canal. The syndrome consists of diplopia from homolateral paralysis of the abducens nerve, pain in the temporoparietal region, along with a purulent discharge.

Labyrinthitis.—Infection may reach the bony labyrinth by extension of osteomyelitis from the petrous. This results in transmission of the infection to the perilabyrinthine lymph system. This can be an occult mechanism for development of intracranial infections by transmission through the ductus endolymphaticus. The first clinical evidence is the development of an abscess in the subdural saccus endolymphaticus. This, however, is a very rare sequence of extension of infection. In fact, Zange stated years ago that the saccus was infected from a contiguous subdural abscess more frequently than from extension of infection via the endolymphatic duct. This may lead to thrombophlebitis of the communicating dural veins.

Infection of the perilymph space takes place through the oval or round window, particularly the latter, which does not have the protection of a bony plug as does the oval window. Myringitis of the inner or secondary tympanic membrane appears first, and the infection is transmitted to the membranous labyrinth. When this is established, the normal lymph content becomes cloudy with cellular exudate, the membrane itself becomes thickened with edema and exudate, and a similar reaction is seen in the delicate structures of the membranous labyrinth, particularly the organ of Corti. Reissner's membrane may rupture, permitting communication between the cochlear and the vestibular ducts. With the subsidence of the active inflammatory reaction and the resulting organization and scarring, irreversible damage is done to these delicate and physiologically important structures.

The possible routes of extension of infections into the labyrinth have long been recognized. They are summarized by Dean and Wolfe as 1, fistula through the round window; 2, fistula through the oval windows; 3, fistula through the bony capsule developing as a result of necrosis of bone or from trauma (this is most likely to occur through the horizontal canal and through the promontory); 4, blood or lymph vessels; 5, patent haversian canals, especially in infants; 6, from marrow spaces of petrosa to the endosteum of the labyrinth. Purulent exudate was found in the round windows of practically all of the 46 cases they studied. To these should be added those cases in which the labyrinth is invaded along the 8th nerve from infected meninges. This occurs particularly in tuberculous and influenzal meningitis, but may be the result of otic meningitis from the opposite side.

Altmann and Waltner also found that infection invaded the labyrinth predominantly through the windows. They also emphasized the importance of Pneumococcus III in labyrinthitis. Although streptococci are a far more frequent cause of mastoiditis, a large percentage of labyrinthine infections are caused by pneumococci.

INTRACRANIAL COMPLICATIONS

For the convenience of the student the intracranial complications from infections of the face and nose, of the maxilla and mandible, of the paranasal sinuses and the temporal bone are included in this section. The complications include meningitis, subdural abscess, brain abscess, septic thrombosis of one or more of the intracranial venous sinuses, especially the cavernous or superior longitudinal.

Acute infections of the other paranasal sinuses are a much more usual cause of these intracranial complications than those of the maxillary sinus, and meningitis is a more frequent result of such extension than is thrombosis of the venous sinuses.

Insignificant infections of the skin of the face, and particularly of the nares, can produce intracranial infection—meningitis and cerebral abscess resulting from thrombophlebitis. Furuncles developing in the hair follicles of the nares may have such an outcome, as seen in a Registry case. A small furuncle on the tip of the patient's nose, which did not invade the mucosa, rapidly became enlarged. In spite of chemotherapy and hot packs, in four days the patient became unconscious and his temperature was 104°. Blood culture revealed *Staphylococcus aureus*. Death occurred eight weeks after onset from thrombosis of the cavernous sinus. Penicillin had been given, but in inadequate amount (825,000 units in 13 days).

Retrograde thrombophlebitis which eventually involves large venous sinuses, particularly the lateral and cavernous, is among the chief causes of intracranial extension of infection. Direct extension through the inner bony capsule of a bone involved in an osteomyelitic process is a much more common source of meningitis and of subdural abscess. Mention has already been made of this in the discussion of the ethmoidal and sphenoidal sinuses, and of the mastoid, petrous and tegmen tympani of the temporal bone. Infections may also reach the cranial cavity by continuity of structure along the carotid canal, the internal auditory canal, and the ductus endolymphaticus. Fractures of the skull that include fissuring of the cribriform plate of the ethmoid or of any of the aerated bony cavities open a pathway for direct bacterial infection of the cranial contents.

In addition to meningitis and subdural abscess, abscesses of the brain are possible. The temporosphenoidal lobe is the most frequently involved. Abscesses of the frontal lobe are generally the result of osteomyelitis of the frontal, ethmoidal or sphenoidal sinuses. More deeply lying abscesses result from embolic infection. The temporal lobe abscess is usually a complication of middle ear or mastoid infection. The majority of the cerebellar abscesses can be traced to chronic infections of the ear, to injuries of the labyrinth, or are secondary to thrombophlebitis of the sigmoid sinus.

A practical point to remember is that an uncomplicated brain abscess is not necessarily acutely fatal. It is not uncommon for a brain abscess to lie dormant for years and to develop a fibroglial capsule that tends to protect the surrounding normal tissue. It can remain entirely subclinical and be discovered at autopsy, or it can incite a train of symptoms that suggest a brain tumor.

Lateral sinus thrombosis.—The dural blood sinuses differ from other veins of their size in having no muscle coat and valves. The sigmoid portion of the sinus is more frequently involved in thrombosis. The commonest sources are infections of the mastoid and of the labyrinth. In connection with the latter it is well to remember that the saccus endolymphaticus is in close contact with the sigmoid sinus.

Septic thrombosis of the cavernous sinus is caused by furuncle and cellulitis of the nose or upper lip, orbital abscess, osteomyelitis, and paranasal sinus infections. It may also follow thrombophlebitis of the pterygoid plexus in septic pharyngitis. Rosenwold discussed the possibilities of transmission of infection from a diseased nasal septum. He lists five avenues; 1, direct extension through a traumatic dehiscence; 2, through natural bony passages, such as the cribriform plate; 3, an intervening osteomyelitis; 4, retrograde thrombophlebitis, and 5, perineural spaces.

A retrograde thrombophlebitis of the venous tributaries of the cavernous sinus may develop and spread intracranially into the communicating venous sinuses. Softening and suppuration of the clot lead to pyemia and purulent leptomeningitis.

The infection first produces endophlebitis, which is a necessary preliminary to thrombus formation. Since it is a contact infection, the thrombus begins in the portion of the wall next to the bone. The thrombus usually, but not always, results in complete occlusion of the lumen. If there is no infection in the thrombus and if the patient survives for a number of days, organization begins and that may end in complete replacement of the thrombus by vascularized connective tissue—canalization of the thrombus.

It is not unusual for the thrombophlebitic process to extend into other portions of the sinus apparatus including the jugular bulb and the internal jugular vein. The jugular bulb can also be the primary site of the thrombophlebitis by extension of an infection through a very thin floor of the middle ear, or through a developmental defect in the intervening bone.

Involvement of the cavernous sinus is an extension from the lateral sinus or from some of the communicating veins. Because of retrograde extension through the ophthalmic veins, a prominent clinical evidence of thrombosis of the cavernous sinus is exophthalmos and edema of the periorbital tissues.

Wittmaack emphasizes the role, in transmitting infections, of persistent vascular communications between the dura and the lateral sinus, jugular bulb, mucosa of the middle ear, roof of the eustachian tube and the mastoid.

Fatal Intracranial Infections Following Tooth Extractions.—Haymaker analyzed 28 cases at the Armed Forces Institute of Pathology in which death occurred from central nervous system infections following the extraction of teeth. The series did not include cases in which there had already been established osteomyelitis of the jaws. Among the lesions were 8 brain abscesses and 11 instances of sinus thrombosis. The remainder were meningeal infections. Direct spread of infection was encountered most frequently after extractions from the upper jaw, while hematogenous spread occurred more frequently following extractions from the lower jaw. It has been the general experience that fatal complications of dental infections are about twice as frequent when the lower jaw is involved as when the primary lesion is in the maxilla.

Direct spread of the infection to the intracranial cavity occurred in 18 cases. In 8 of these an extending cellulitis produced osteomyelitis of the greater wing of the sphenoid from which there was direct intracranial involvement. In 7 of the 9 instances of sinus thrombosis, infection reached the sinus through the venous blood stream. In the remaining 2 there was direct extension to the sinus from infected bone. There were 6 instances of intraorbital abscess. Of paranasal sinuses involved, the sphenoidal was most frequent and the maxillary next.

The diagram in the following plates traces the venous connection between the teeth and the cavernous sinuses. It will be noted that infections from the anterior teeth reach the sinus via the anterior facial and the ophthalmic veins, and those from the posterior teeth reach the ophthalmic veins through the pterygoid plexus. The frequency of the involvement of the ophthalmic vein probably accounts for the high incidence of orbital infections.

THE EFFECTS OF TRAUMA ON THE MIDDLE EAR AND TEMPORAL BONE

An important industrial hazard is introduced when individuals are exposed to repeated or sustained noises; riveters and artillerymen are prominent examples. In extreme cases the bony transmission apparatus is subject to trauma which leads to disruption and fibrosis of the important articulations between the incus and stapes and the foot plate of the stapes and the oval window. There may be actual fracture of the ossicles. The real damage, however, is not likely to be to these comparatively robust structures, but it always includes the delicate components of the labyrinth. Reissner's membrane, for example, may be ruptured, but usually only its hair cells are destroyed along with their sustentacular cells and other parts of the organ of Corti.

Of less serious purport are the difficulties of persons who are subjected to wide variations in atmospheric pressure. It is only with violent changes and air emboli that there is damage to the delicate components of the membranous labyrinth.

Aerotitis Media (Otitic Barotrauma).—This is an entity that became better understood during World War II with the development of high-altitude flying. Clinically, it had been known for years, for it occurred in caisson workers, divers, and submarine personnel. While the disease is due largely to alterations in atmospheric pressure, animal experiments have suggested that other factors may be involved, particularly oxygen deficiency or oxygen poisoning from too high a concentration in the inspired air.

The condition was first described and named aero-otitis media by Armstrong and Heim. They attributed it to failure of ready ventilation through the eustachian tube and called attention to the etiologic importance of any condition that compromised the lumen of the tubes.

In acute cases there is hyperemia of the mucous membrane if the pressure is in the negative phase, and ischemia if it is in the positive phase. The mucous membrane later becomes congested and swollen from edema, there is more or less desquamation of epithelium, and there may be an exudation of serous or serosanguineous fluid into the cavity of the middle ear. There is no suppurative element. The tympanic membrane is congested and it can be ruptured.

With repeated exposures to the causative conditions a chronic inflammatory element characterized by mononuclear exudate is added to the picture. Since the eustachian tube shares in this reaction, a vicious circle is established if flying is continued.

Haynes and Harris have called attention to the same condition arising in submarine personnel. The incidence is lower, however, and the reaction is less severe than in aviators.

In the large amount of material received at the Institute during the war, largely through the efforts of E. P. Fowler, Jr., it was found that hemorrhages were a prominent feature. These hemorrhages from the mucosa of the middle ear were into the cavity and into the tissues of the round window, occasionally involving the membranous labyrinth. These hemorrhages were not the result of trauma but were from pressure variation or possibly from anoxia. Our material came principally from aviators who died at high altitudes under circumstances which interfered with the pressurizing of the cabin of the plane or with the supply of oxygen. Most of these aviators had had many hours of flight at very high altitudes. This material, therefore, affords opportunity to determine any morphologic evidence of reaction to the mechanical conditions of such activity. The study revealed several instances of otosclerotic changes. It is most likely, however, that these were coincidental rather than the direct result of flying conditions. It is difficult to appraise the changes in the labyrinth because the conditions under which the material was obtained were not always conducive to the perfect fixation which is necessary to preserve these delicate structures. Several examples of the early otosclerotic changes are included in the illustrations. The reaction is practically limited to the rim of the oval window and to the foot plate of the stapes.

Otologists are recognizing more and more the incidence of aerotitis media from flights in commercial planes and even in those who travel in automobiles over mountainous areas, especially if they are suffering from colds.

TUMORS OF THE TEMPORAL BONE

Among the benign tumors of the temporal bone one of the commonest is exostosis about the internal auditory meatus. Hyperostoses are occasionally seen in the mastoid. Dermoid cysts, nevus, fibroma, chondroma and hemangioma are rare tumors of the temporal bone.

Lederer lays considerable stress on endothelioma of the middle ear. This seems like an over-emphasis and possibly reflects a misinterpretation of inflammatory tissue. He states that it appears clinically as an infectious otitis with a bloody discharge, swelling over the mastoid, possible facial paralysis and regional lymph node involvement. The lesion presents as firm resisting granulations.

Primary carcinoma of the middle ear is very rare. In practically every instance there has been a history of a prolonged chronic suppurative otitis media. The most common site of origin is the fundus of the external meatus and the temporal bone is involved as a result of extension by continuity and by invasion of the cancellous bone. Schlittler reported in 1919 on 83 primary carcinomas that he had collected from literature.

The commonest point of origin is the margin where the squamous epithelium normally becomes the mucosa of the middle ear. The fact that squamous cell carcinoma does occur in the middle ear indicates that there has been a preliminary metaplasia of the normally more cuboidal epithelium of this part.

According to Goerke, the one instance of cylindrical cell carcinoma reported some time ago proved to be metastatic rather than primary. So far as can be determined there is no authentic instance of primary carcinoma of the middle ear that has retained its more respiratory type of cell. We have no instance of adenocarcinoma occurring in the middle or inner ear among the material in the Registry.

Carcinoma of the middle ear gives no particular diagnostic clinical evidence. There may be facial paralysis and evidence of the involvement of the structures in the middle and inner ear. Bleeding is more common than with the benign lesion and it would be an important point in differentiating carcinoma from cholesteatoma. Tuberculosis must also be eliminated before carcinoma can be considered.

Carcinoma of these parts is much more frequently an EXTENSION from the neighboring structures, especially from the external ear, the external auditory canal, the parotid gland, the paranasal sinuses, the eustachian tube, pteryogomaxillary fossa, sphenoid recess, epipharynx, and from structures in the neck.

There have been occasional instances of blood or lymph-borne METASTASIS from distant parts, especially from the prostate. Here the cancellous bone and the bony capsule are apt to be involved rather than the cavities. In other cases, the canals of the cochlea may be filled with tumor cells and the bony spiral invaded. There are other instances of metastasis from carcinoma of the uterus and breast and from hypernephroid tumors of the kidney. These metastases from distant parts are usually accidental findings, and no doubt routine examination of temporal bones would reveal a higher incidence than is realized from clinical evidence.

Sarcoma, while rare, is more frequently found in the temporal bone and its contents than is carcinoma, but here again it is usually secondary, either by extension or by metastasis. These tumors, especially the osteogenic ones, may reach great size.

Kelemen reported an instance of carcino-sarcoma, but there is no similar tumor in the Registry. Invasion of the cavities in the temporal bone by **meningioma** from the intracranial meninges occurs rather frequently. Tumor cells, carried by the spinal fluid, can also gain access to the basal coil of the cochlea through the internal meatus, according to Denker.

The temporal bone is involved in **leukemic infiltrations**, and an example is included in the illustrations. In this instance it was discovered by biopsy and was the source of the primary diagnosis of the blood disease.

Another complication of leukemia, particularly the acute forms, are hemorrhages into the inner ear, with or without infiltrations by the leukemic elements. In chronic leukemias there is occasionally massive degeneration of the 8th nerve. Tumor may obliterate blood vessels and thus produce anemia of the labyrinth. It is a matter of historic interest that Ménière's case with bilateral hemorrhages into the inner ear probably was myelogenous leukemia. Chloromatous infiltrations that involved the periosteum and dura have also been reported.

In the terminal cachexia of malignancy there may be toxic degeneration of the structures of the inner ear, at times associated with inflammatory reaction.

Neurofibroma of the auditory nerve is the commonest tumor associated with the hearing apparatus, in fact, it is one of the commoner of the intracranial tumors, constituting about a sixth of the group. It is usually unilateral, but involvement of both nerves is not unusual. Occasionally, it is associated with general peripheral neurofibromatosis (von Recklinghausen's disease) in which the other stigmata of the complex may be present, particularly the café au lait spots on the skin. Henschen made a special study of this tumor and reported that he could find no difference in sex incidence, and that it occurred at all ages, most commonly between 20 and 50 years. Of 240 cases that he reported, 22 were bilateral. The reason that the tumor occurs so commonly in the region of the 8th nerve is that the origin is in an embryonal developmental disturbance in the region of the distal portion of the 8th nerve, either characteristic of this nerve, or having a predilection for this region. The origin is completely extraglial. It is of the same nature as von Recklinghausen's fibromas that also depend on the presence of a mixture of embryonal neurogenous anlagen. Should it be called a hamartoma?

Neurofibroma very rarely occurs in the region of the cochlea. The tumor is an expansile benign growth of the sheath of the 8th nerve. It arises in the nerve near the vestibular ganglion in the internal auditory canal, expands into the cranial cavity, and can reach a diameter of 5 or more centimeters. Occassionally it expands into the cochlea. It comes eventually to lie in the cerebellopontine angle. The 7th nerve is at times included as the tumor expands but the 5th nerve is usually first involved.

The histologic features are the same as those of other neurofibromas, as described under the general pathology of tumors. There too the still unsettled histogenesis of the group is discussed; whether they are neurectodermal and therefore neurilemomas, or whether they are of fibrous tissue elements of the nerve and therefore mesenchymal and properly called neurofibromas.

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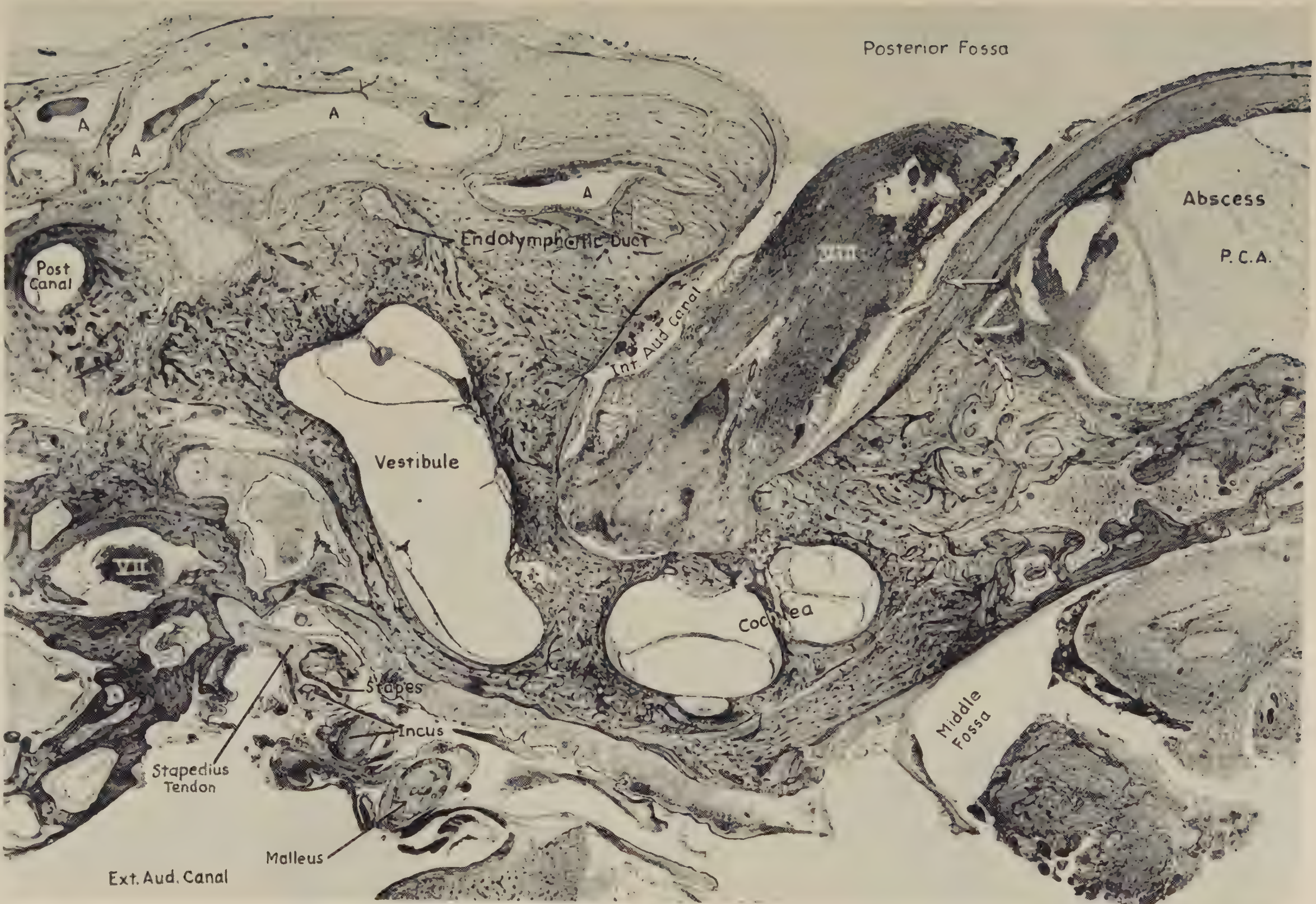
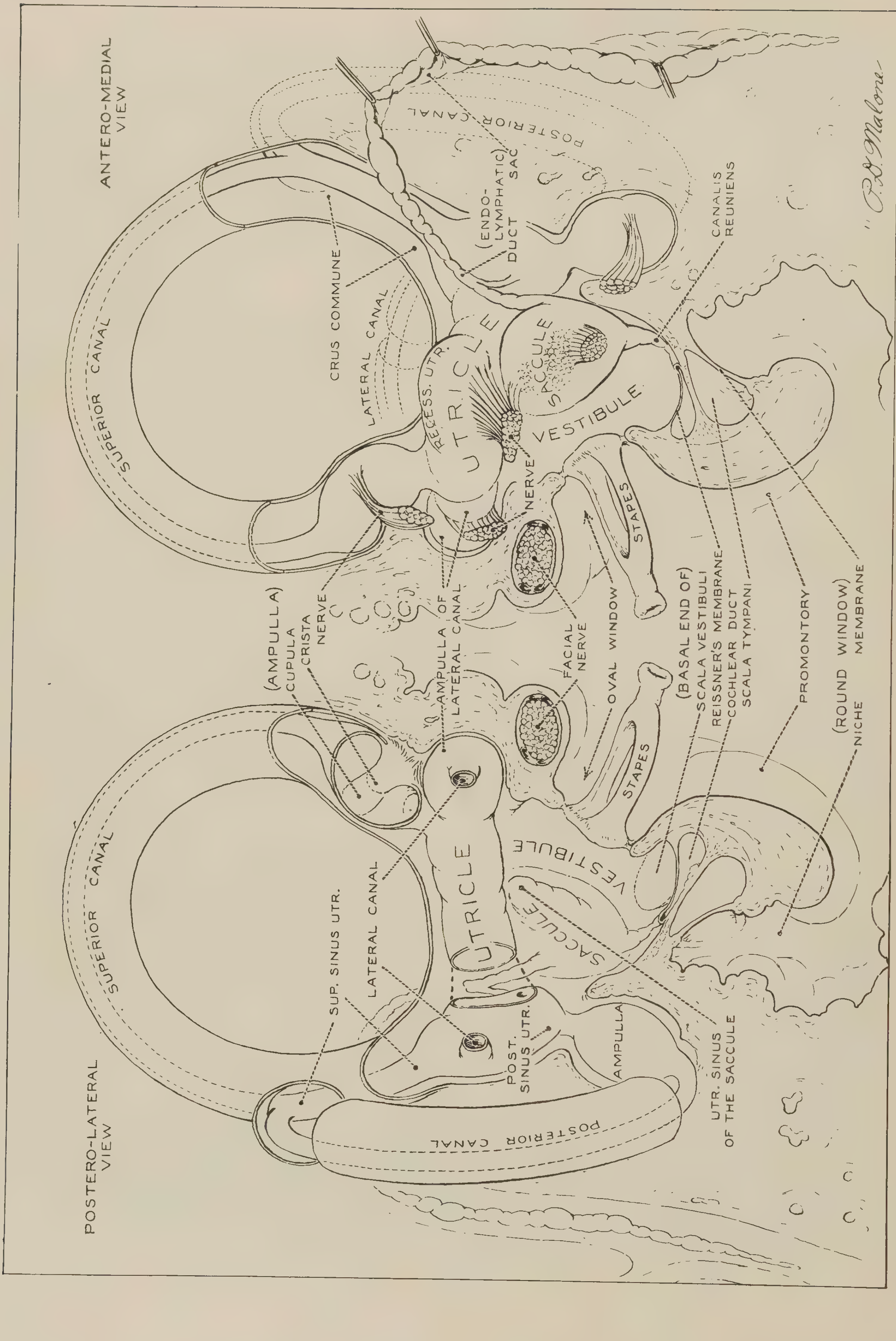
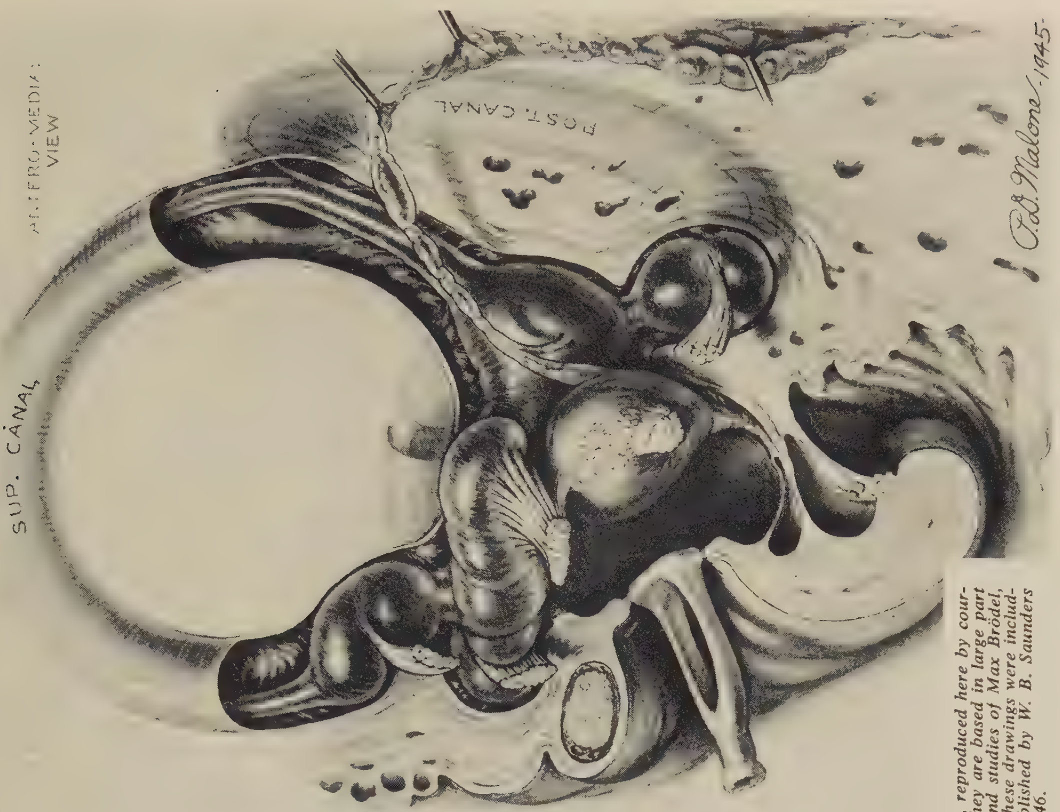
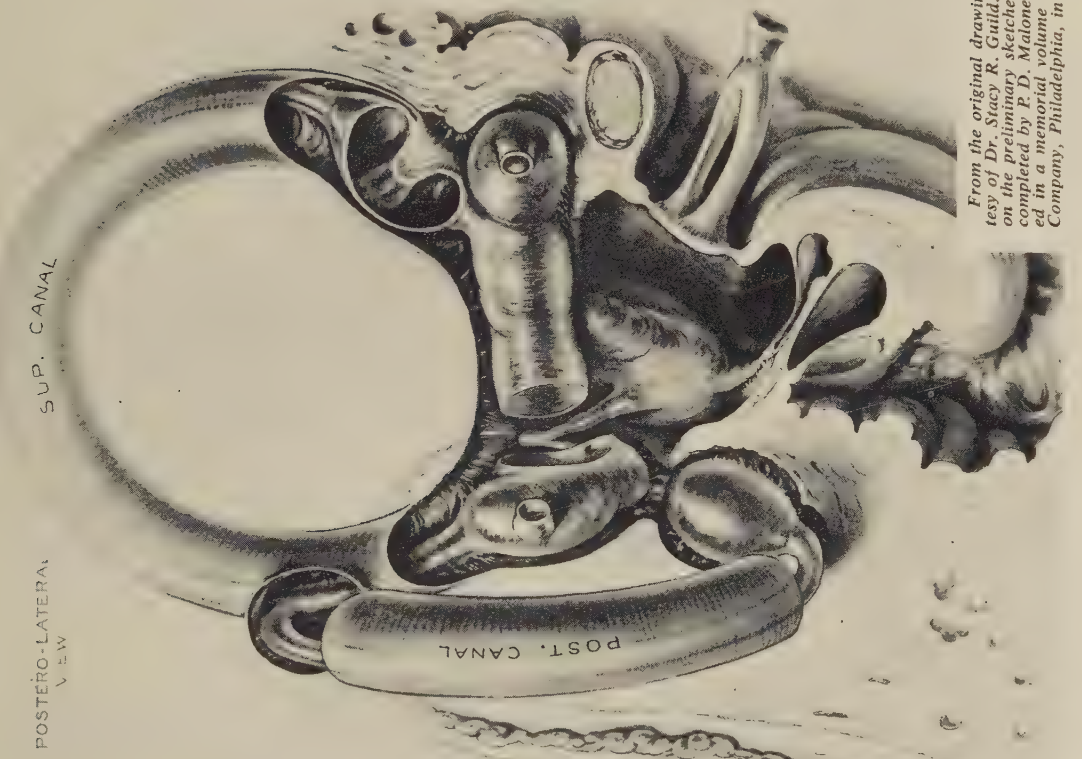

Posterior Fossa
A
A
A
A
Abscess
P.C.A.
Post Canal
Endolymphatic Duct
VIII
Int. Aud. Canal
Vestibule
VII
Cochlea
Stapes
Incus
Stapedius Tendon
Middle Fossa
Malleus
Ext. Aud. Canal

Petrositis, resulting from chronic otitis media in a 42 year old woman on whom mastoidectomy had been performed five days after onset of earache on the right. A week following operation, she complained of headache, and pain developed in the right cheek and eye; two weeks later, paralysis of the sixth and seventh cranial nerves on the right. Death from meningitis.

Horizontal section through internal auditory meatus. Mucosa of middle ear and pneumatic cells is edematous and congested; exudate in middle ear and air cells. Chain of small pneumatic cells marking pathway of infection from the mastoid to the petrous air cells are lettered **A**; abscess that developed in a large pneumatic cell in petrous apex, **P.C.A.** *Arrow* indicates the point of erosion (not shown in this section) of the abscess into the internal auditory canal. Pus fills the canal, infiltrating the eighth nerve, and has extended to adjacent meninges. (J.R. Lindsay, Chicago, Ill.)


POSTERO-LATERAL VIEW
ANTERO-MEDIAL VIEW
SUPERIOR CANAL
CRUS COMMUNE
LATERAL CANAL
(ENDO-LYMPHATIC) DUCT SAC
POSTERIOR CANAL
CANALIS REUNIENS
RECESS. UTR.
UTRICLE
SACCULE
VESTIBULE
NERVE
STAPES
(AMPULLA) CUPULA
CRISTA
NERVE
AMPULLA OF LATERAL CANAL
FACIAL NERVE
OVAL WINDOW
(BASAL END OF) SCALA VESTIBULI
REISSNER'S MEMBRANE
COCHLEAR DUCT
SCALA TYMPANI
PROMONTORY
(ROUND WINDOW) NICHE
MEMBRANE
SUPERIOR CANAL
SUP. SINUS UTR.
LATERAL CANAL
UTRICLE
VESTIBULE
SACCULE
POST. SINUS UTR.
AMPULLA
UTR. SINUS OF THE SACCULE
STAPES
POSTERIOR CANAL
P.D. Malone

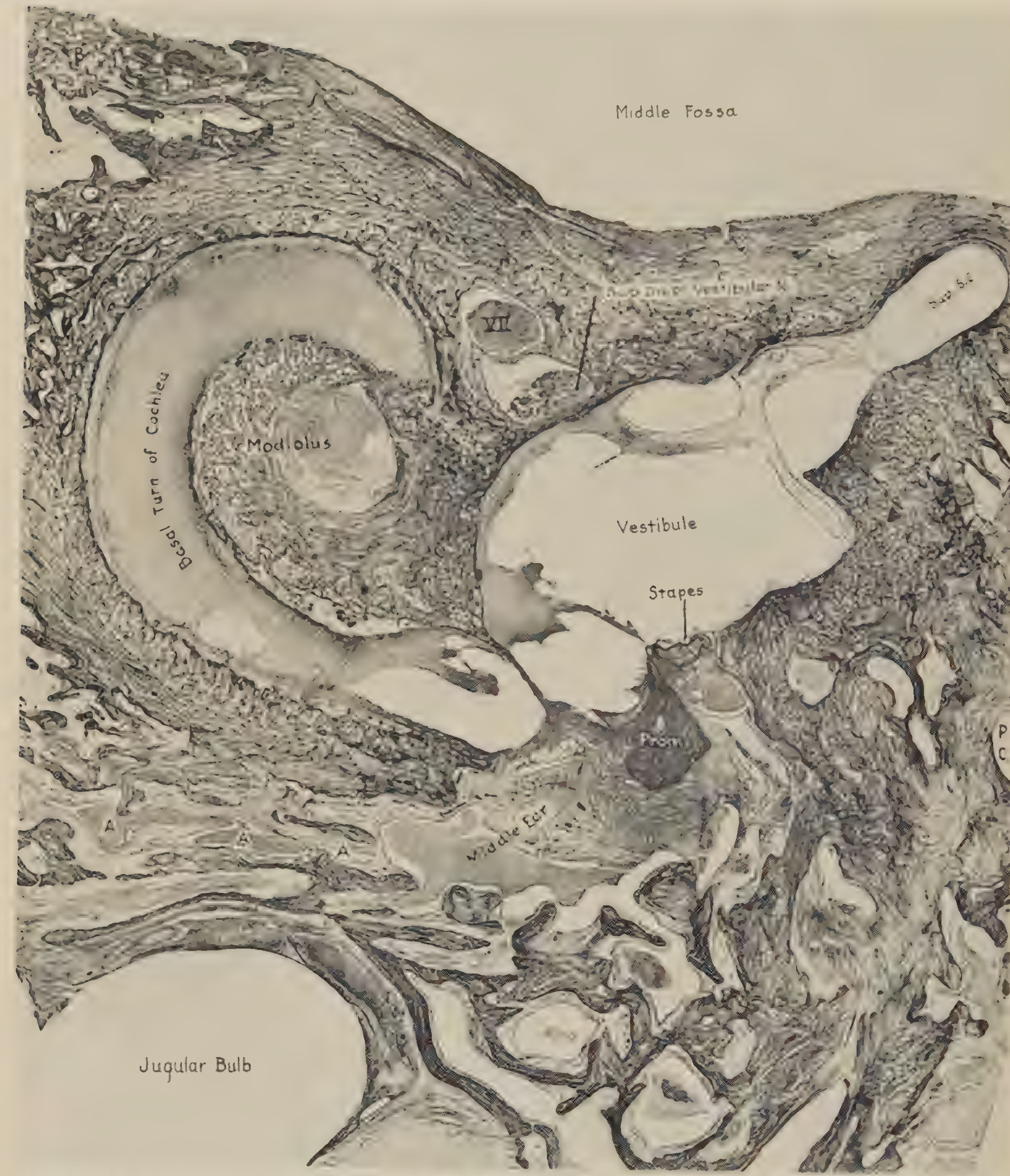

ANTERO-MEDIAL VIEW
SUP. CANAL
POST. CANAL
P.D. Malone. 1945.


POSTERO-LATERAL VIEW
SUP. CANAL
POST. CANAL

From the original drawings, reproduced here by courtesy of Dr. Stacy R. Guild. They are based in large part on the preliminary sketches and studies of Max Brödel, completed by P. D. Malone. These drawings were included in a memorial volume published by W. B. Saunders Company, Philadelphia, in 1946.

LABYRINTHITIS

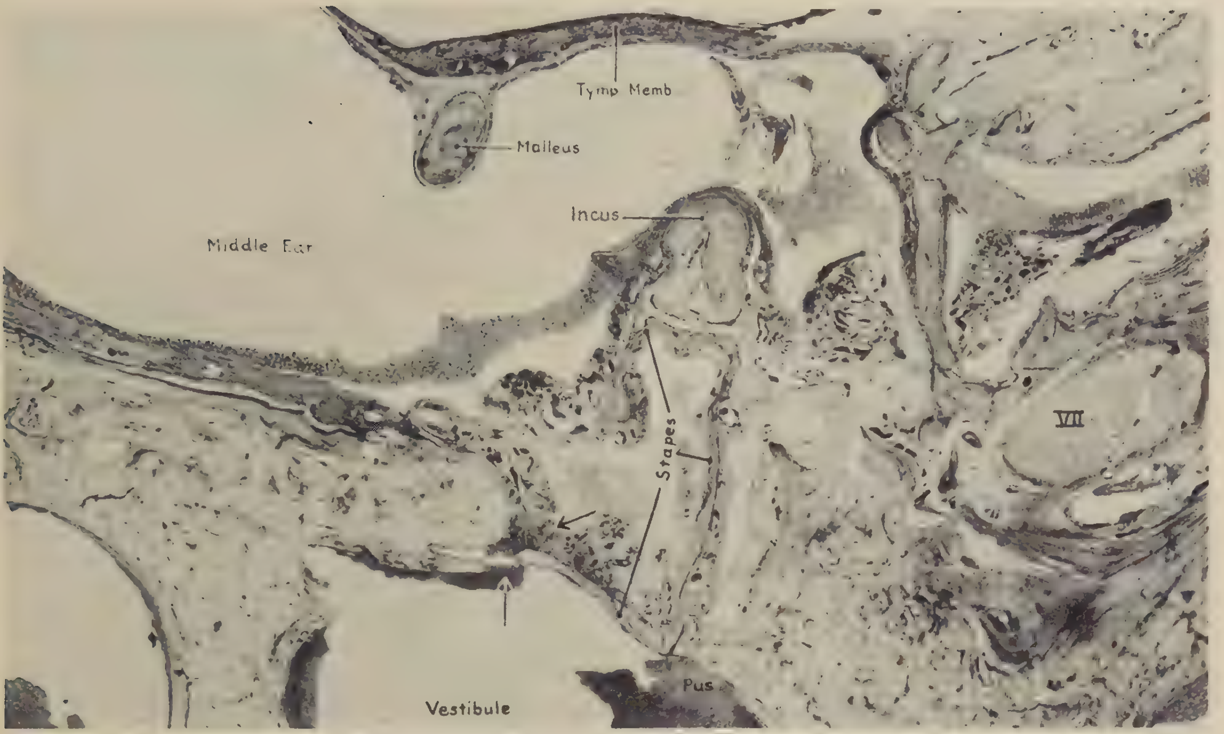
FOLLOWING PURULENT INFECTION OF THE MIDDLE EAR



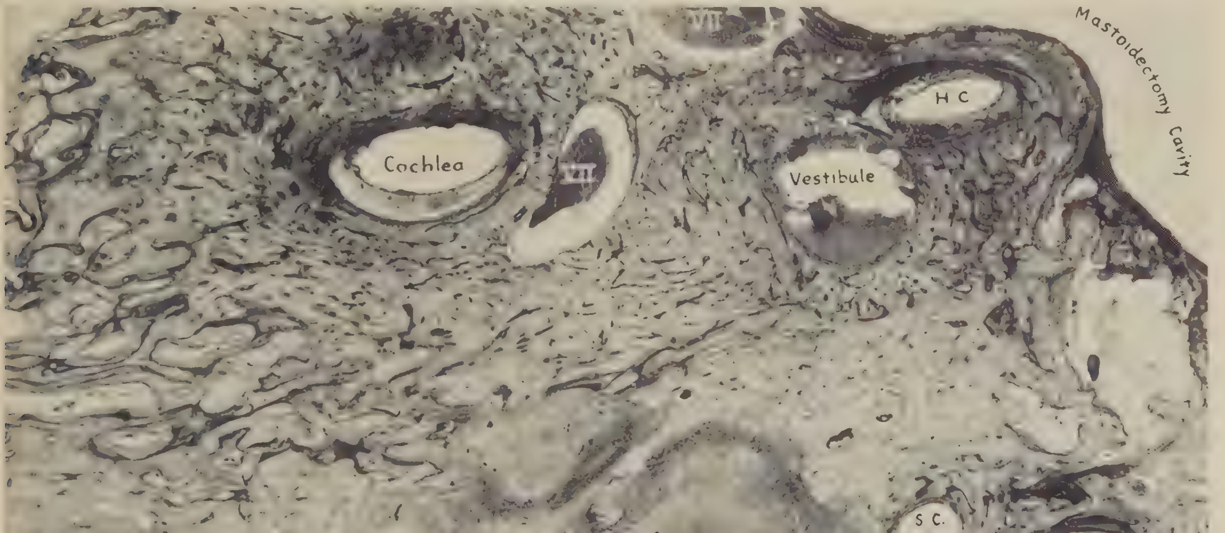
Labyrinthitis of probable tympanogenic origin in a 6 year old boy. Onset with pain and discharge from right ear, impaired hearing and vomiting; three weeks later, sudden violent dizziness and vomiting for five days; two days later definite signs of meningits; no improvement after mastoidectomy; death six weeks after onset.
Middle ear and basal turn of cochlea filled with pus; purulent exudate in vestibule. Note severe involvement of windows, particularly the round window, which is the probably primary pathway of extension in this case. Primary tympanogenic labyrinthitis through the windows as portal of entry may follow acute otitis media or an acute exacerbation of chronic otitis media. Interpretation is difficult since histologic changes in the windows secondary to a labyrinthitis from other portals are usually identical. (H. Altmann.) Infected hypotympanic cells marked "A" represent pathway of extension to petrous apical abscess (not shown) which eroded into meninges. New bone formation (**B**) in focus of osteitis adjacent to abscess. (J.R. Lindsay, Chicago, Ill.)

LABYRINTHITIS

TYMPANOGENIC–FOLLOWING BONE EROSION


Tymp Memb
Malleus
Incus
Middle Ear
Stapes
VII
Vestibule
Pus

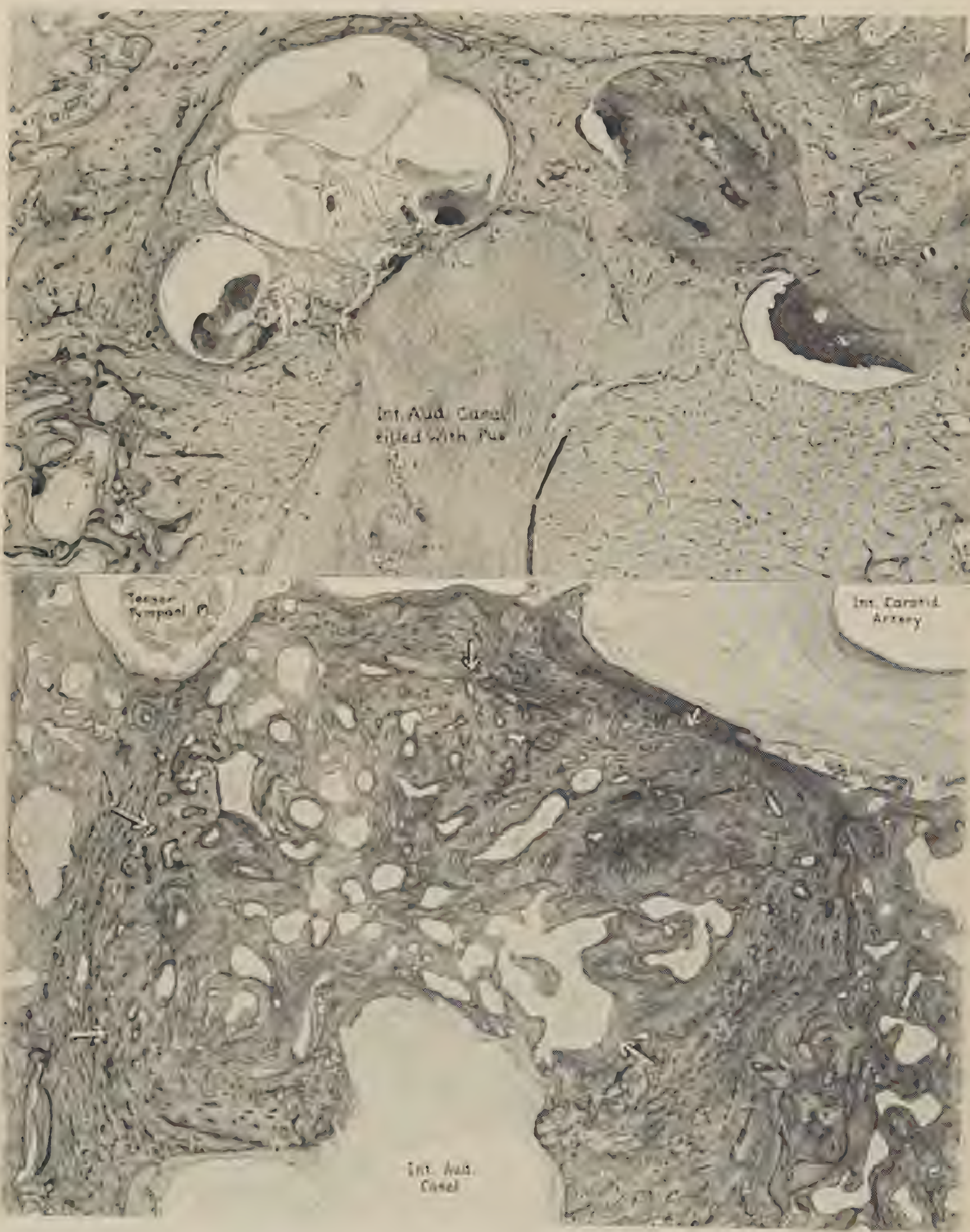
Labyrinthitis due to direct extension of purulent exudate into vestibule through oval window, in a case of severe suppurative otitis media. Granulation tissue and dense purulent exudate surround stapes. The annular ligament has been destroyed, and through this area *(arrows)* purulent exudate has extended into vestibule from middle ear. (E.P. Fowler, Jr.)


VII
Mastoidectomy Cavity
HC
Cochlea
VII
Vestibule
Abscess
S.C.
Posterior Fossa
Dura

Labyrinthitis due to erosion of a perilabyrinthine abscess into superior semicircular canal *(arrow)*. The labyrinthitis resulted in meningitis and death. Case of chronic osteomyelitis of petrous pyramid in a patient who had a discharging ear for twenty years. Note that the abscess has also broken through the cortex to the dura, but that the dura is thickened and intact. (E.P. Fowler, Jr. and P.H. Swenson).

LABYRINTHITIS

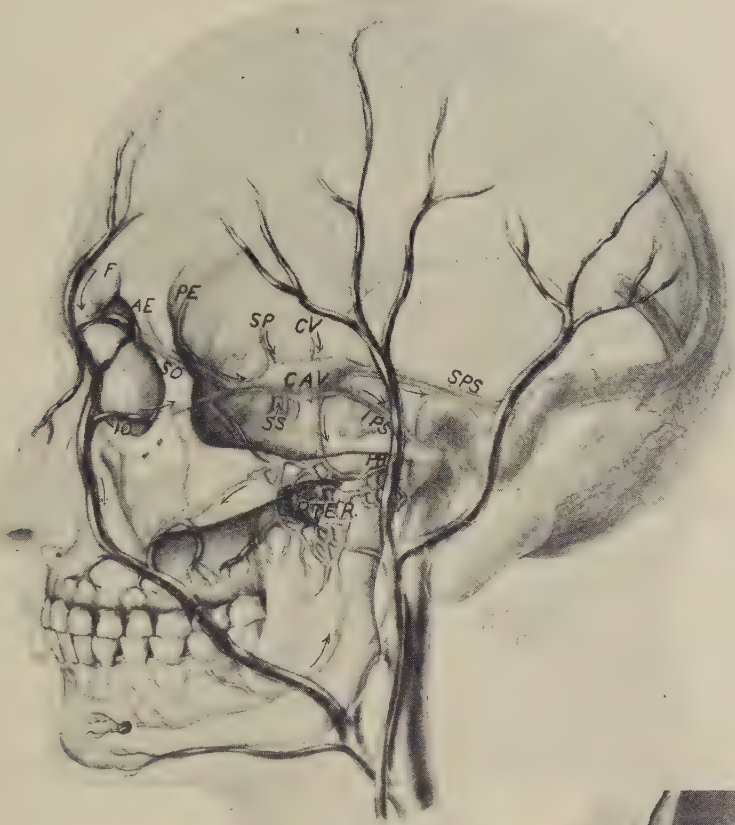
FOLLOWING MENINGITIS


Int. Aud. Canal
filled With Pus
Tensor Tympani M.
Int. Carotid Artery
Int. Aud. Canal

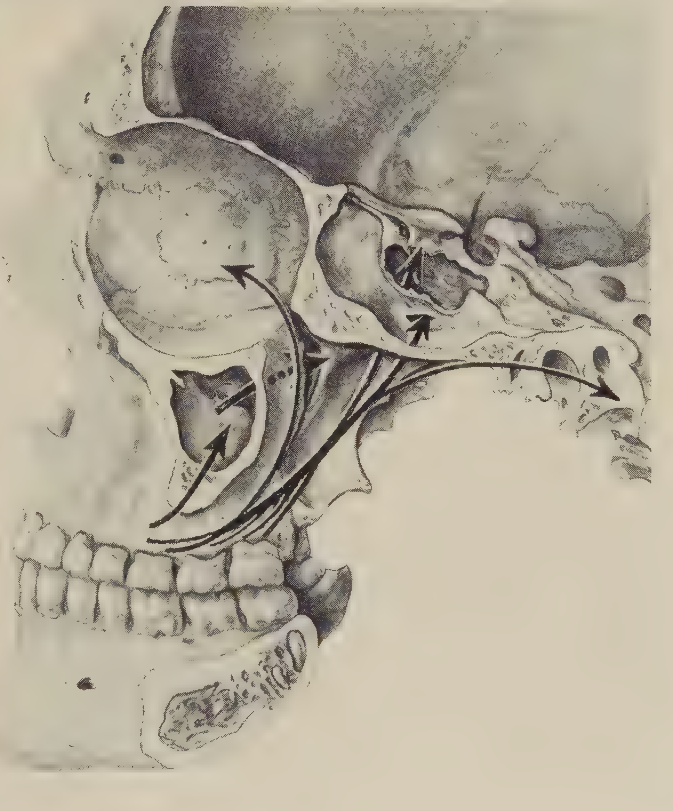
Upper: **labyrinthitis due to extension of suppurative meningitis into the internal auditory canal.** Internal auditory canal filled with purulent exudate from meningeal infection. Partial destruction and suppuration of cochlea at base. Purulent exudate in cochlea and vestibule. x29. (F. Altmann and J.G. Waltner, N.Y.)

Lower: **obliterative labyrinthitis of long duration, following meningitis.** Entire cochlea, the margins of which are indicated by *arrows,* is replaced by dense bone. Mid modiolar section. x22. (S.R. Guild.)

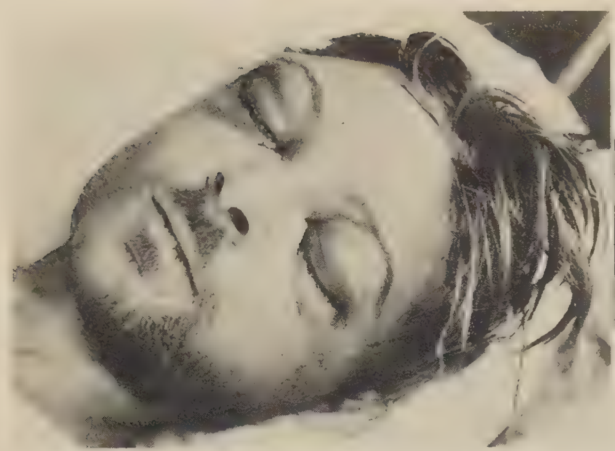
PATHWAYS OF INFECTION TO INTRACRANIAL CAVITY



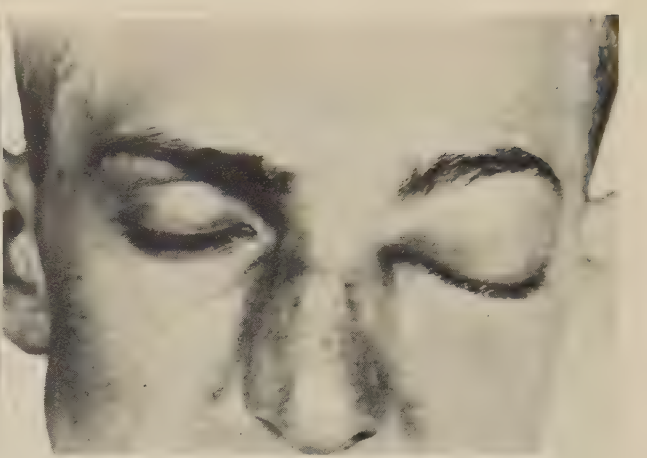
Osseous and Direct Pathways of Ascending Infection from Jaws to Intracranial Cavity *(below).* Most frequent site of penetration of base of skull, particularly by infections complicating tooth extraction, is greater wing of sphenoid near foramen ovale (arrow). The extracranial collection of pus may be so deeply situated that its presence is not recognized clinically. Next most frequent structures involved are the sphenoid sinus and overlying sella turcica. Infection may reach sphenoid sinus directly (indicated by arrow within exposed sphenoid sinus) or by contiguity from greater wing of sphenoid. A sphenoidal sinusitis may also result from retrograde thrombosis from a thrombosed cavernous sinus. Another route of spread is through petrous part of the temporal bone. In some cases, infection reaches the retrobulbar tissues, and then may enter the intracranial cavity via ophthalmic veins or by direct spread through orbital fissure or canal. (Both from W. Haymaker, Wash., D.C.)



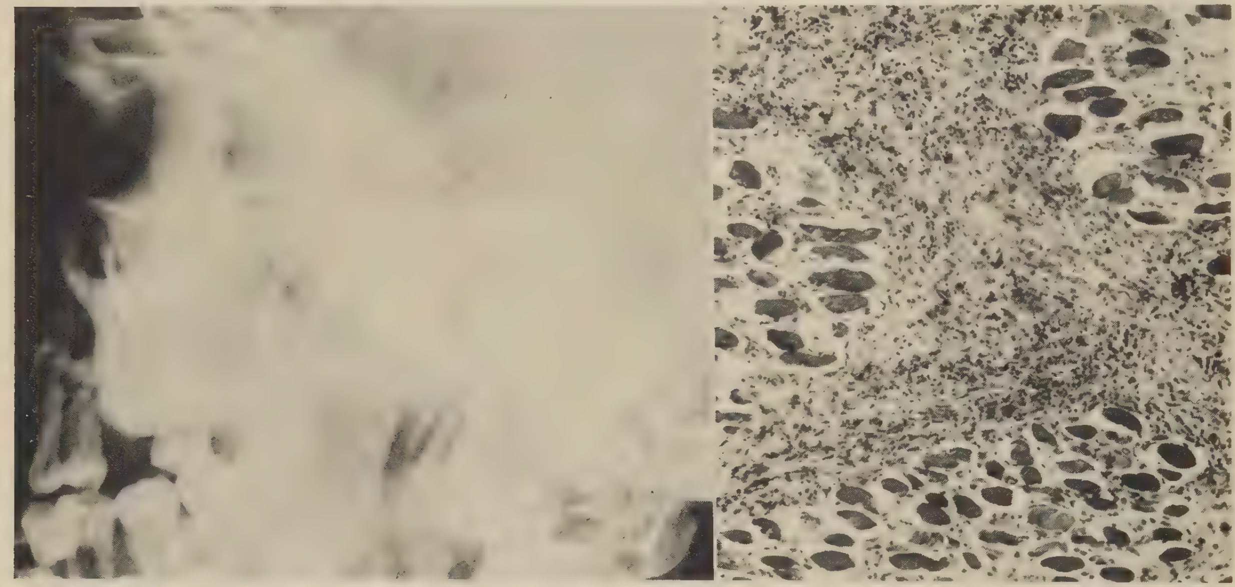
Venous Pathways—the Venous Tributaries of the Cavernous Sinus *(above).* Deeper veins, pale grey; superficial ones, darker color. Arrows indicate direction of blood flow. Veins of lower jaw drain via inferior central vein into pterygoid plexus (PTER); veins from upper jaw and facial structures drain in two directions: the more anterior into anterior facial vein, the more posterior into pterygoid plexus. The pterygoid plexus drains teeth, fauces, soft palate, and pharynx. Infections from it reach cavernous sinus by way of vein of Vesalius; foramen ovale and foramen lacerum; or veins communicating with inferior ophthalmic vein (IO). Anterior route to cavernous sinus occurs via anterior facial and angular veins, and then through orbit by way of ophthalmic veins, especially the superior (SO). These veins drain anterior facial structures (external nose, lips, forehead, eyelids, cheek) and mucosae of frontal sinuses (F); ethmoidal cells (AE and PE), and upper lateral nasal wall. Cavernous sinus also receives venous blood from mucosa of sphenoid sinus (SS); from superficial inferior cerebral veins (CV); and from sphenoparietal venous sinus (SP), which drains diploe of lesser wing of sphenoid and veins of dura mater.



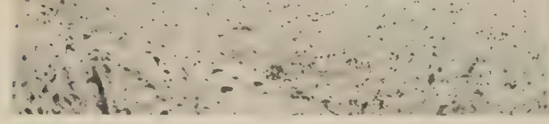
Bilateral cavernous sinus thrombosis following sinusitis, nasal polypectomy and extraction of right molar tooth. Marked edema of both orbits and face, left exophthalmos.



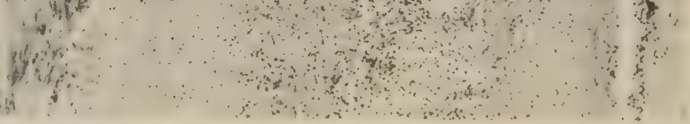
Cavernous sinus thrombosis, left, following sinus infection in 28 year old man. Marked edema and discoloration about left eye. Death with meningitis and brain abscess.



Cavernous sinus thrombosis (same case as *upper left*). Death with suppurative pansinusitis, severe bilateral osteomyelitis of bones of face and skull, extensive meningitis and multiple brain abscesses. Roentgenogram shows only focal destructive process in left maxilla. *Right:* extensive pharyngeal cellulitis. x90.

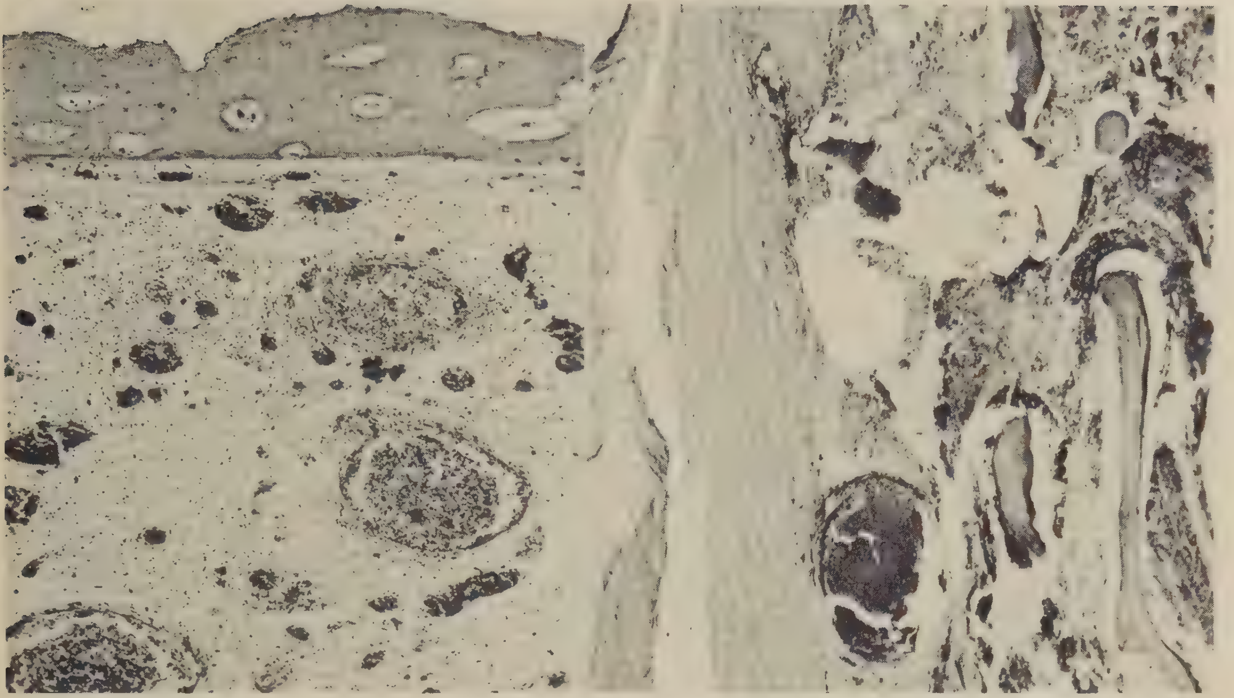


Thrombophlebitis of leptomeningeal vein at base of pons in the same case. Note purulent exudate in wall of vessel. x100.

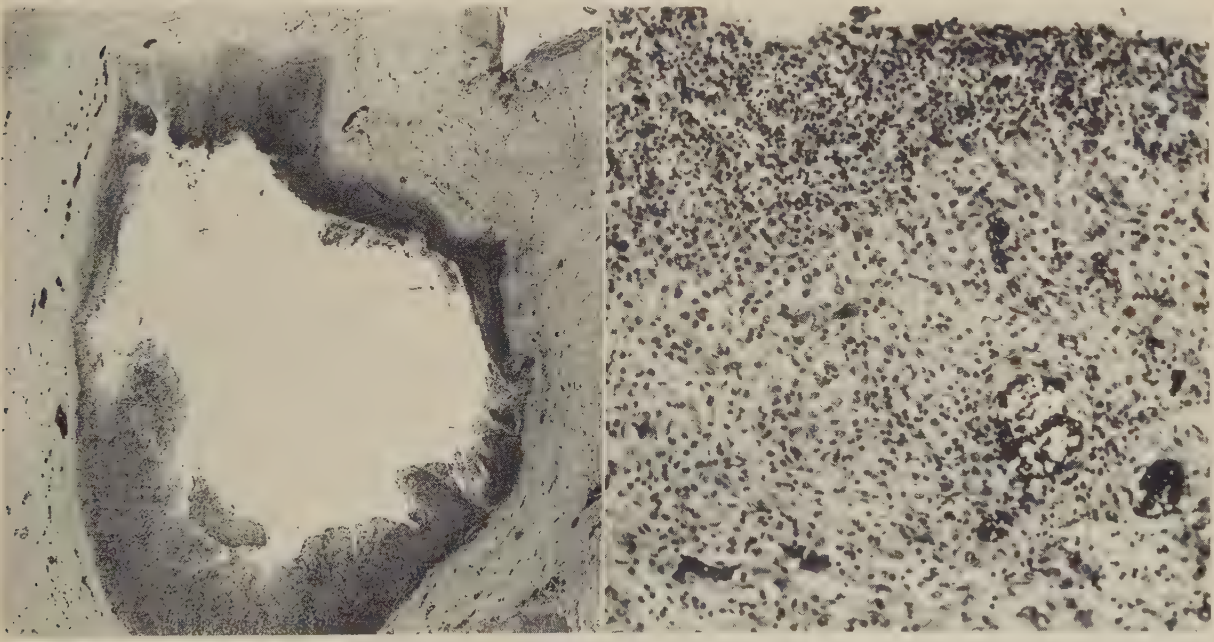


Thrombosis of superior petrosal sinus. Fibrinopurulent thrombus. Dural wall is essentially normal. x100. Similar thrombi in other sinuses.

COMPLICATIONS FROM INFECTIONS OF FACE, SINUSES, AND TEETH



Bilateral sinus thrombosis (cavernous, circular, petrosals, lateral), same case as preceding plate. Death with suppurative **pansinusitis; osteitis** and **osteomyelitis** of bones of face and skull; **abscesses**—maxillary, periorbital, temporal, epidural and perihypophysial; thrombosis of angular vein; **subdural empyema;** suppurative **meningitis.** *Left:* **purulent thrombophlebitis,** greatly thickened edematous mucosa of sphenoid sinus (one of important pathways of infection to cranial cavity). x75. *Right:* **purulent osteitis** of greater wing of sphenoid bone (another important site in direct osseous spread of infection to cranial cavity).



Brain abscess, one of many due to hematogenous spread of infection. Death with bilateral sinus thrombosis secondary to furuncle on tip of nose. *Left:* abscess of frontal lobe. Circumscribed collection of pus in white matter well below cortex. Very thin fibroblastic outer layer seen only at left. x8. *Right:* wall of abscess: outer zone (at bottom) of gliosis with macrophages and fibroblasts; middle zone of granulation tissue with mononuclear and compound granule cells; inner purulent zone with leukocytes, some erythrocytes and necrotic debris. x125.

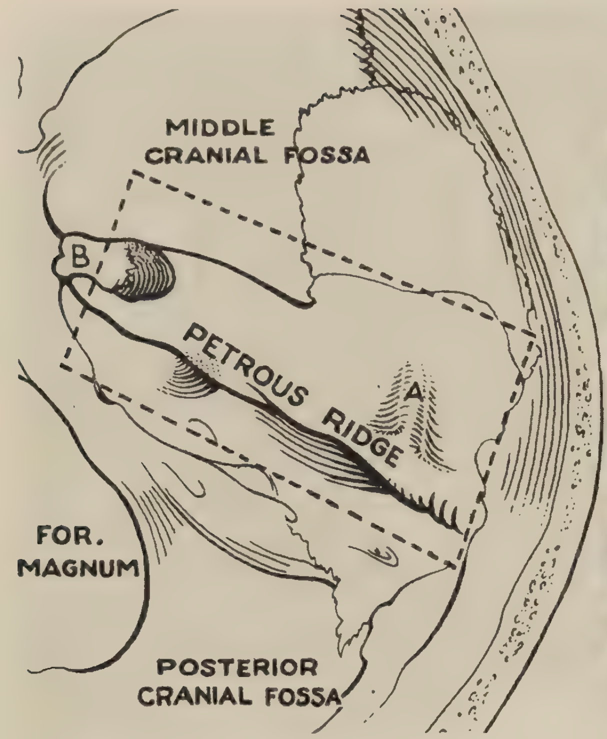
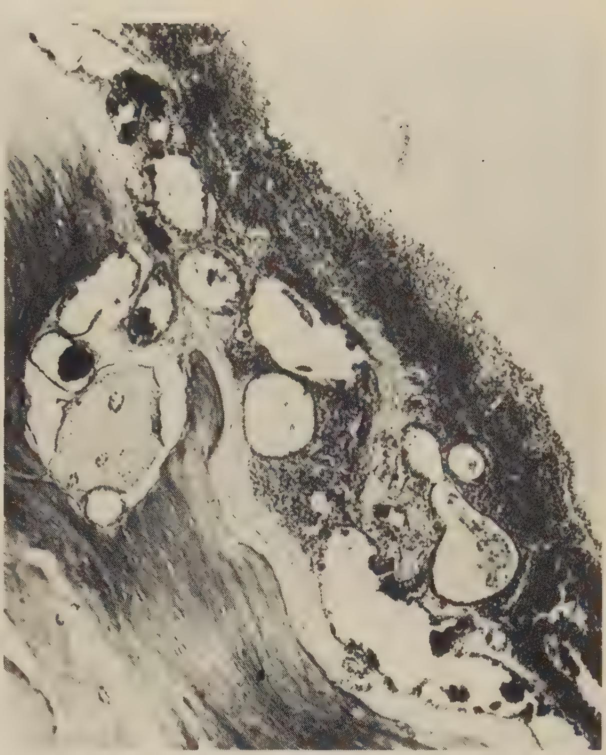
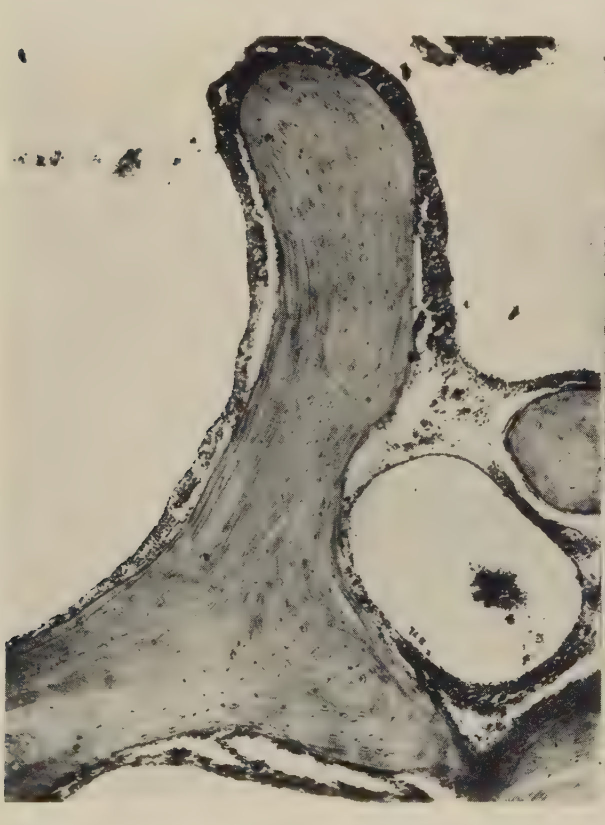

MIDDLE CRANIAL FOSSA
B
PETROUS RIDGE
A
FOR. MAGNUM
POSTERIOR CRANIAL FOSSA

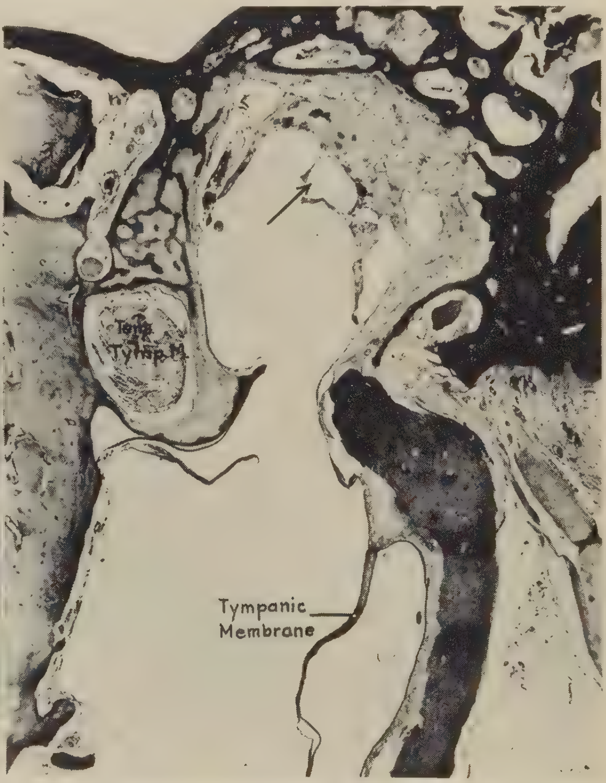
Diagram outlining temporal bone block to be removed for adequate histologic preparation and study. **A,** eminence of superior semicircular canal; **B,** carotid canal.



Acute aerotitis, severe. Death from anoxia at high altitude. Pronounced vascular congestion and extensive hemorrhage into the mucosa of the middle ear of an aviator. x70.

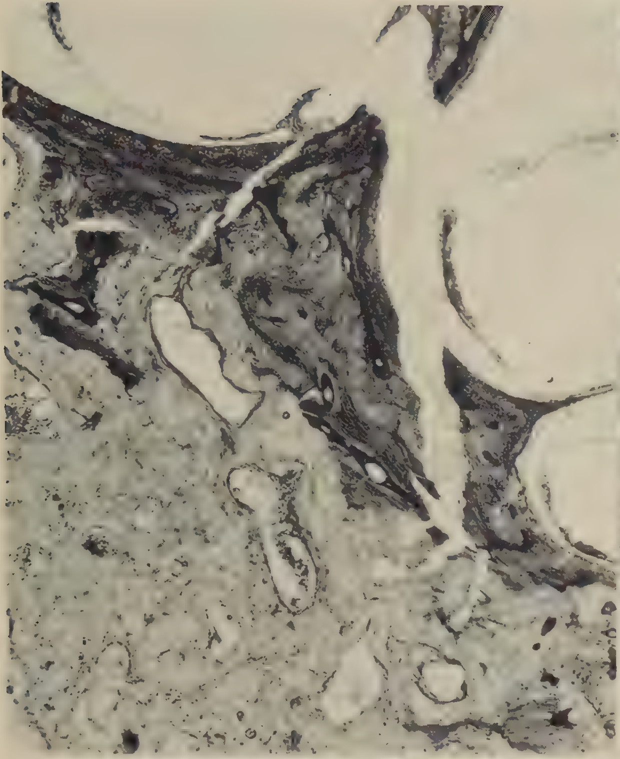


Hemorrhage due to anoxia in mucosa of mastoid air cells. Young aviator. x95.

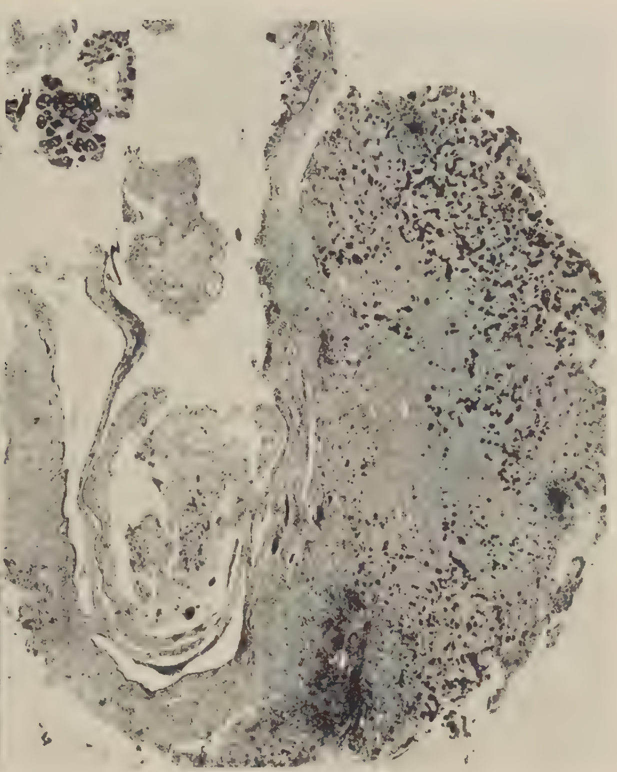

Tens. Tymp. M.
Tympanic Membrane

Aerotitis, chronic, mild. Organized and organizing exudate in epitympanum *(arrow)*. x40.

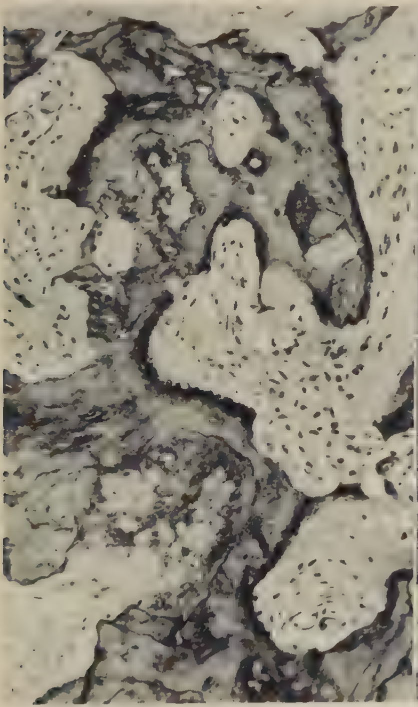
PAGET'S DISEASE, TEMPORAL BONE
BENIGN BONE TUMORS



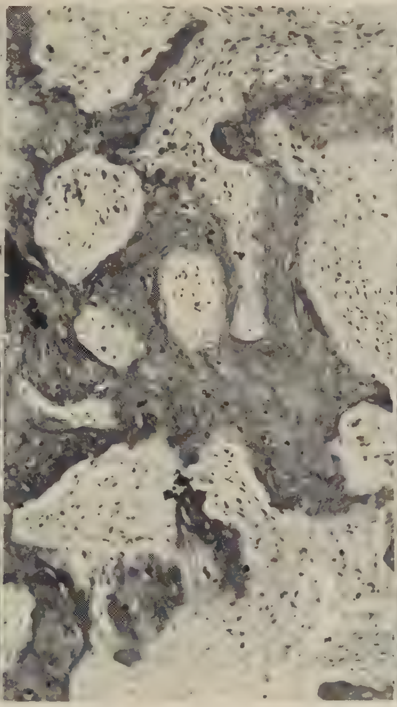
Early Paget's disease with focal involvement of lamellar endosteal bone of the otic capsule is sharply contrasted with normal adjacent enchondral bone. (E.P. Fowler, Jr.)



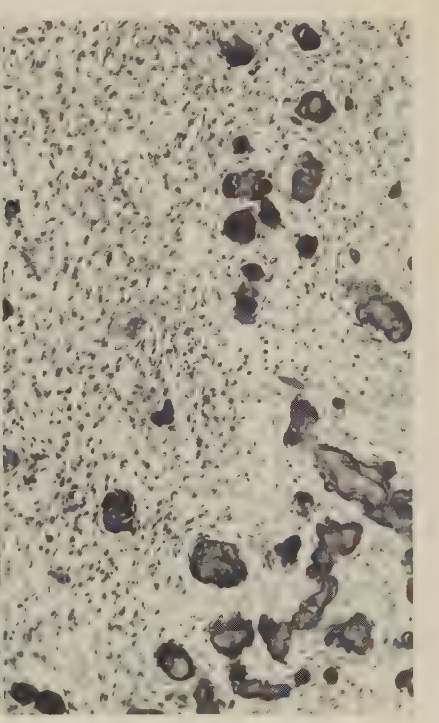
Ossifying fibroma, mastoid, noted in roentgenograms of temporal bone of 14 year old boy. Similar to that seen in maxilla. x21. Magnified field at *lower right.*



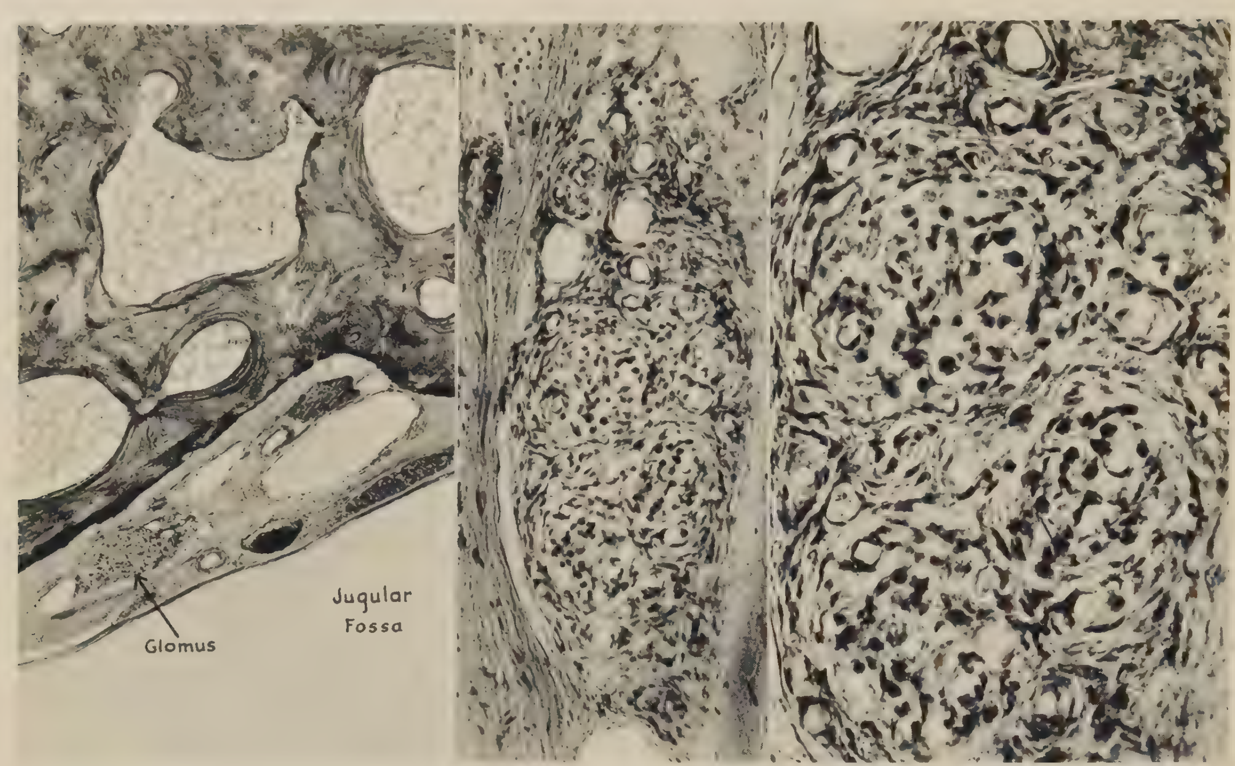
Paget's disease. Prominent cement lines and irregularly resorbed margins produce typical mosaic pattern. x125.



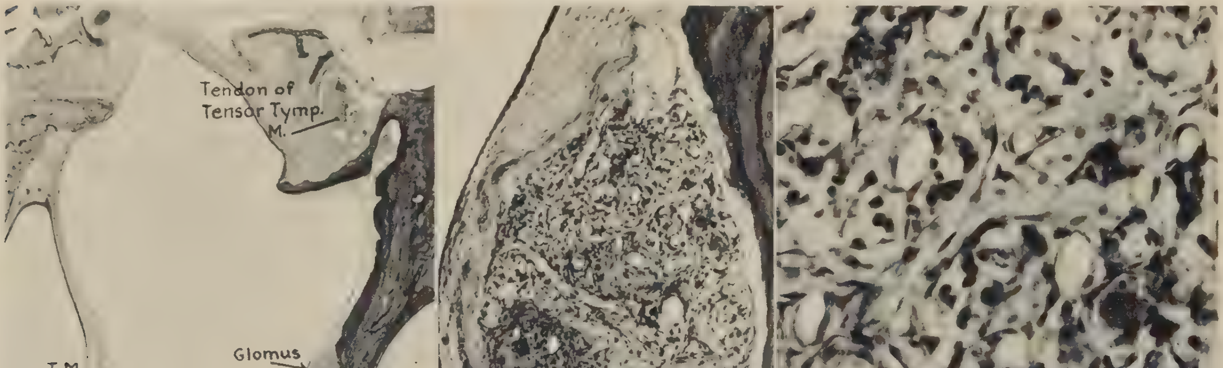
Osteoma, temporal bone of young man, to illustrate difference in lamination of trabeculae. x125.



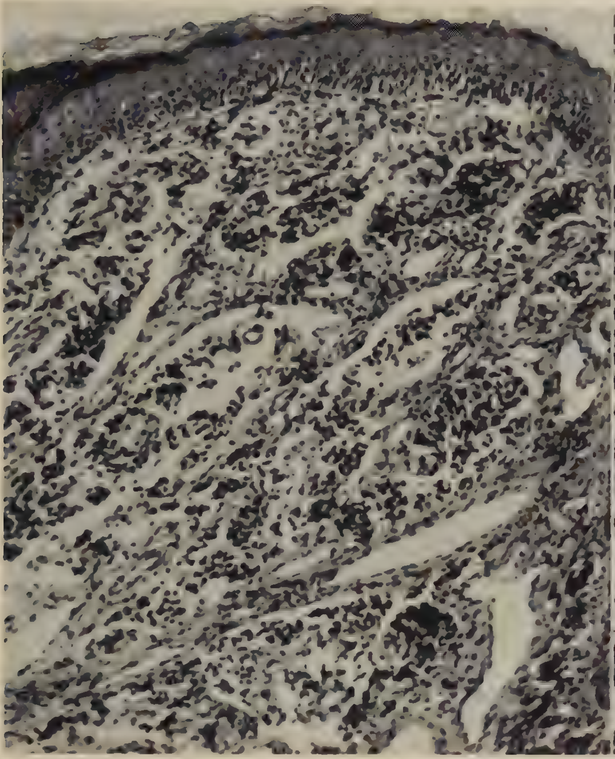
Ossifying fibroma. Cellular fibrous background with many small and irregular bone trabeculae. x125.



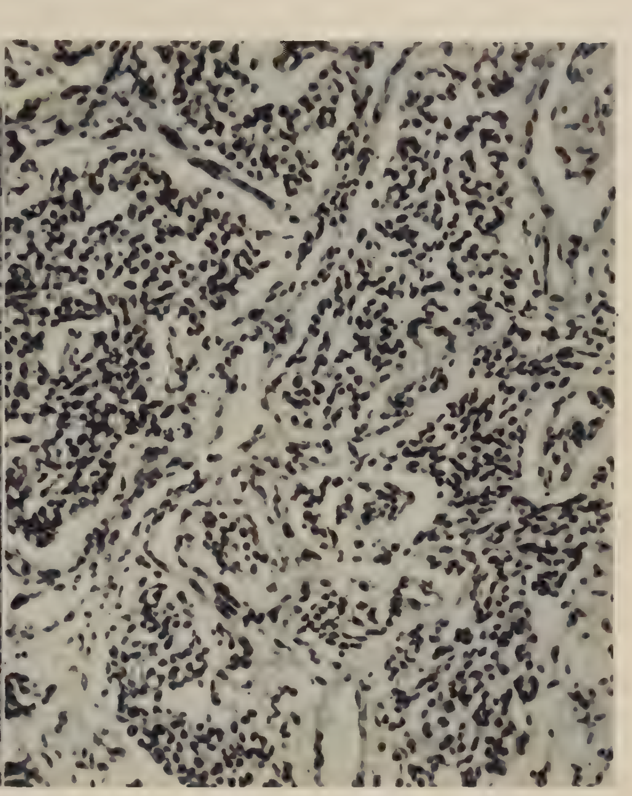
Glomus jugulare. A nonchromaffin paraganglion, (described by Guild in 1941) typically situated in the adventitia of the bulb of the jugular vein immediately below the bony floor of the middle ear. Closely related vessels and bundles of nerve (glossopharyngeal) fibers. Composed of "capillary vessels and numerous epithelium-like cells between the vessels." This body appears more cellular than the paraganglion illustrated *below*. x32, x165, x360.



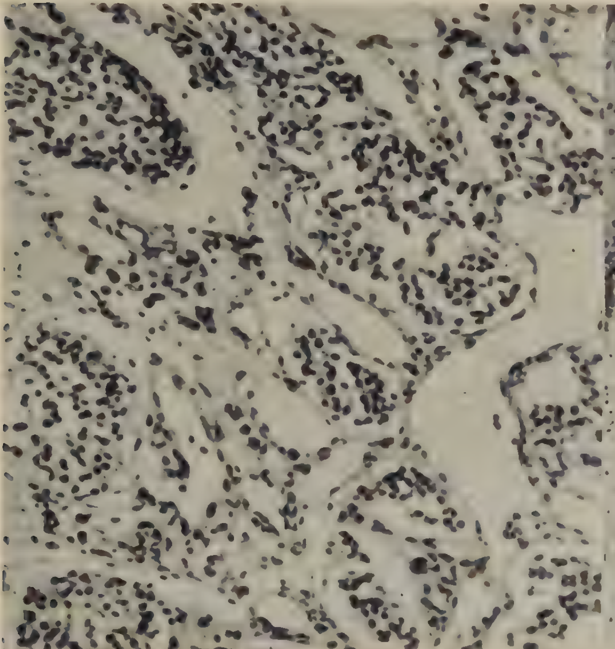
Paraganglion tympanicum (glomus tympanicum), within the mucosa of the middle ear over the promontory, closely associated with the tympanic branch of the glossopharyngeal nerve. Note afferent artery (tympanic branch of ascending pharyngeal artery) and efferent vein; prominent vascular structure within the glomus. x10, x90, x315.



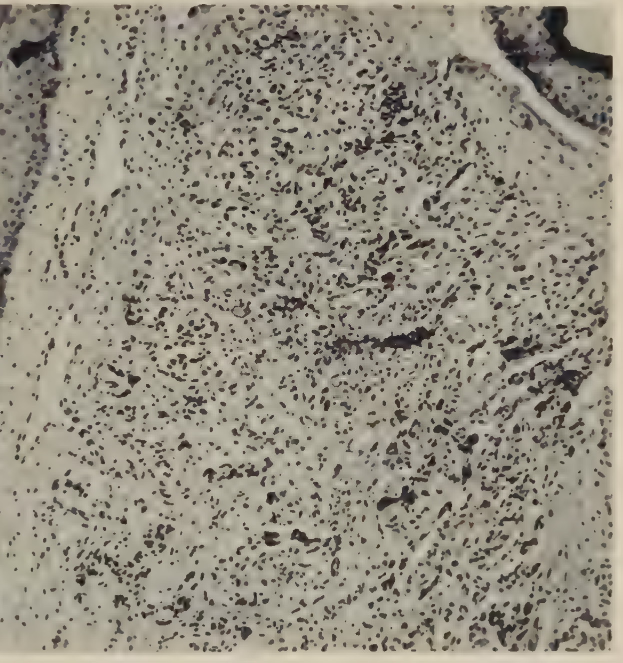
Tumor diagnosed hemangioma, presented as recurrent "aural polyp" in the external auditory canal of a 55 year old woman with increasing deafness for five years. Profuse hemorrhage followed incision. Radical mastoidectomy. x125. (W.D. Gill, San Antonio, Tex.)



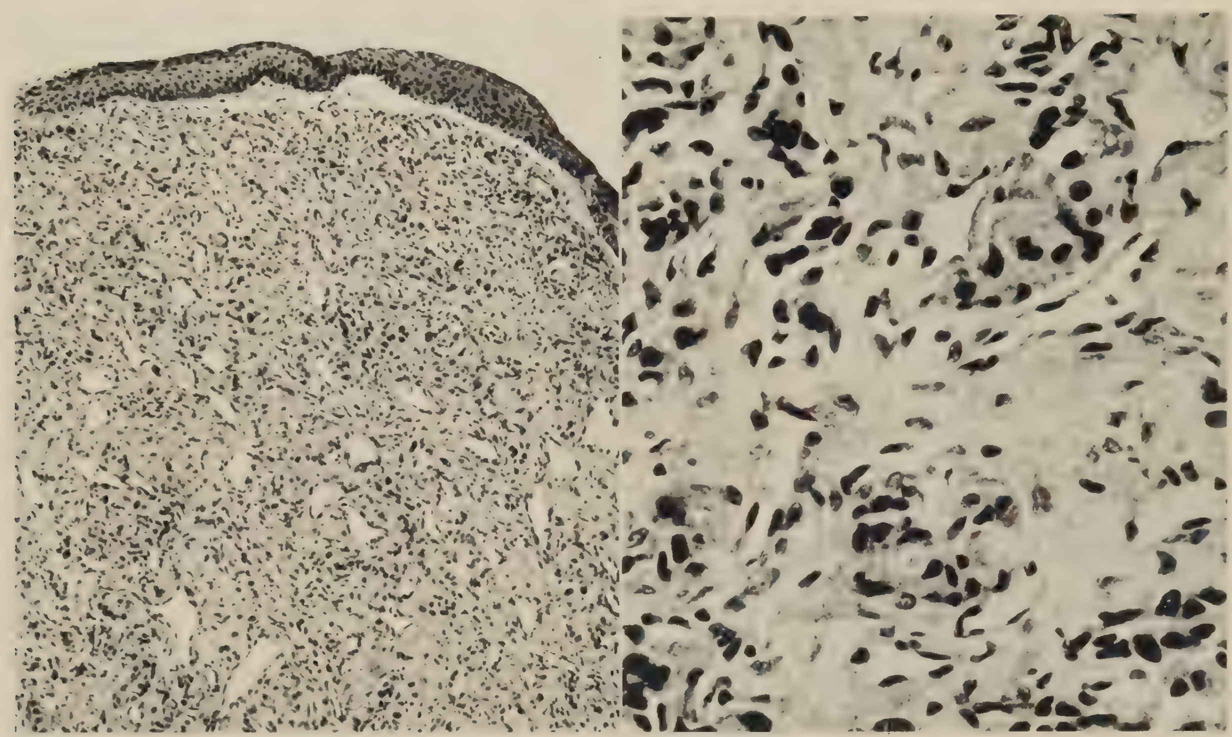
Cellular field from same tumor. Solid masses and anastomosing cords of cells in groupings larger than in the normal glomus jugulare. Composed of cells, fairly uniform in size, closely associated with capillary vessels, some of which are collapsed. x165.



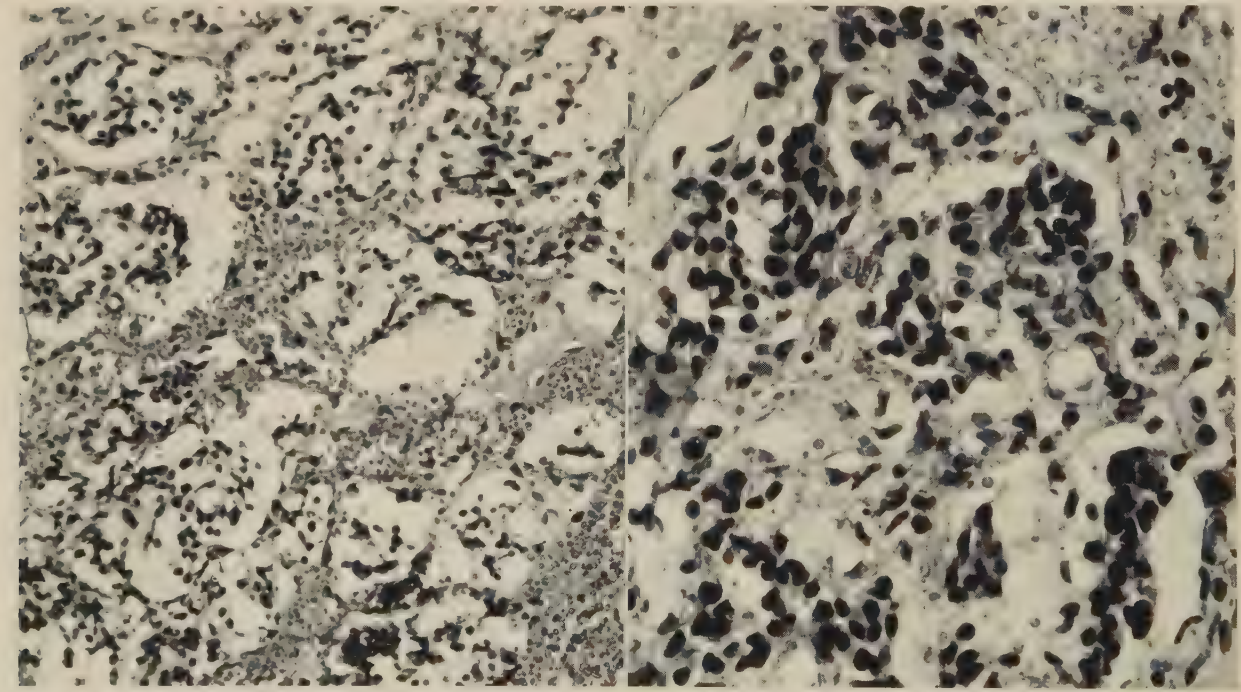
Striking vascular pattern in another field from the same tumor is accentuated by the dilatation of the thin-walled vessels. Spindle shape of cells and scant cytoplasm, in this case, are partly due to poor fixation of specimen. x210.



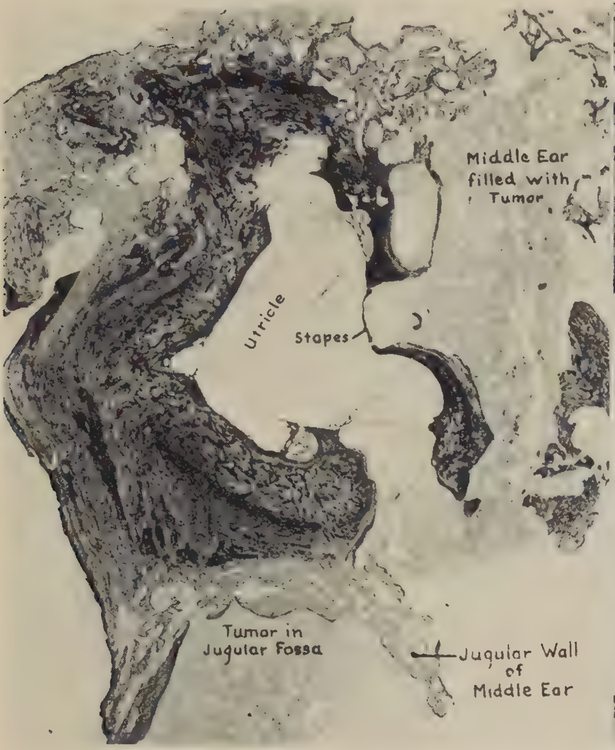
More abundant stroma in a less cellular tumor presenting in the external auditory canal of an adult male. Initial diagnosis was carcinoma because of variation in size of cells, some with large bizarre hyperchromatic nuclei. x90.



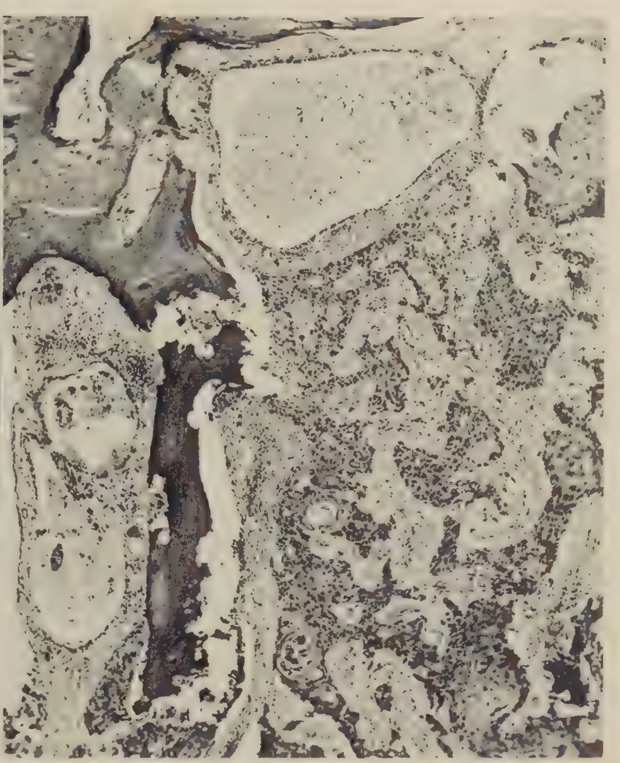
Glomus jugulare tumor presenting in external auditory canal of a 53 year old man was removed at the time of resection of a mass in the neck that proved to be a carotid body tumor. The two tumors had the same organoid structure and cytologic features. Nests of "epithelioid" cells with vesicular or hyperchromatic nuclei and abundant granular eosinophilic cytoplasm closely associated with thin-walled blood vessels. x91, x400. Other cases of nonchromaffin paraganglioma with multicentric origin have been reported. (M.C. O'Donnell, Santa Monica, Calif.)



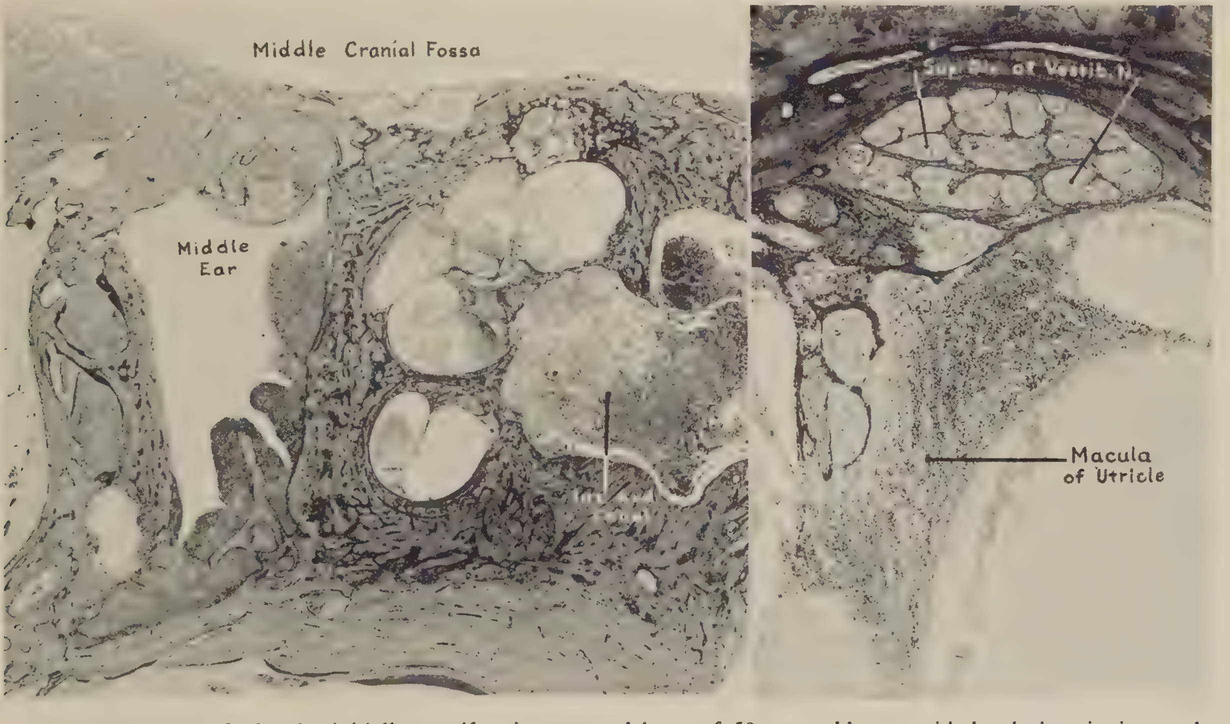
Glomus jugulare tumor in radical mastoidectomy specimen from a 58 year old man with slowly progressive deafness, tinnitus, tenderness over the mastoid and a "bulging canal containing granulation tissue so that the drum could not be seen." Profuse hemorrhage at operation from vascular tumor that filled middle ear and mastoid and extended through drum to external auditory canal. Note nests of cells that appear to project into the vascular spaces. x165, x400.


Middle Ear filled with Tumor
Utricle
Stapes
Tumor in Jugular Fossa
Juguiar Wall of Middle Ear

Meningioma from the cranial cavity has filled the jugular fossa, and through the jugular wall invades and fills the middle ear. The inner ear is normal. x5. (S.R. Guild.)

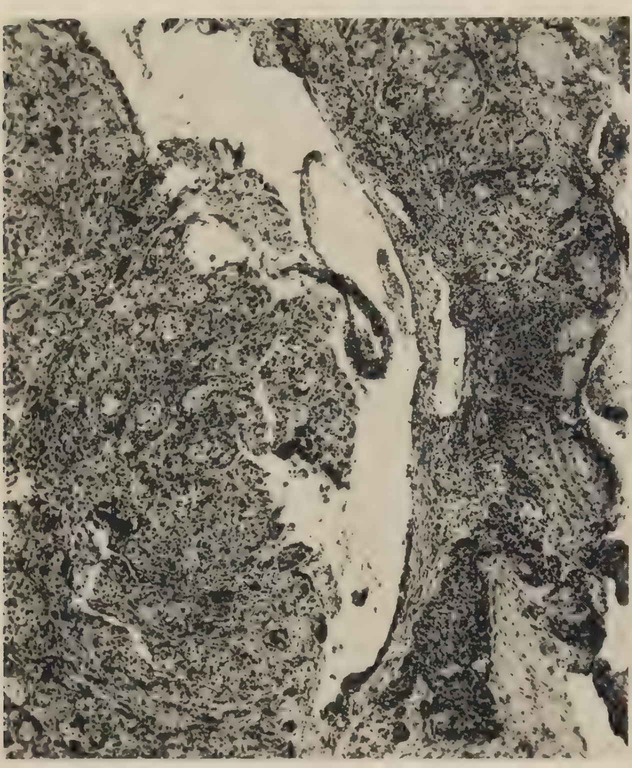


Epidermoid carcinoma, primary in external ear, has invaded temporal bone. Infiltrating well differentiated tumor about air cells at top and left. Note osteoclasis and fragmentation of petrous bone. x48.

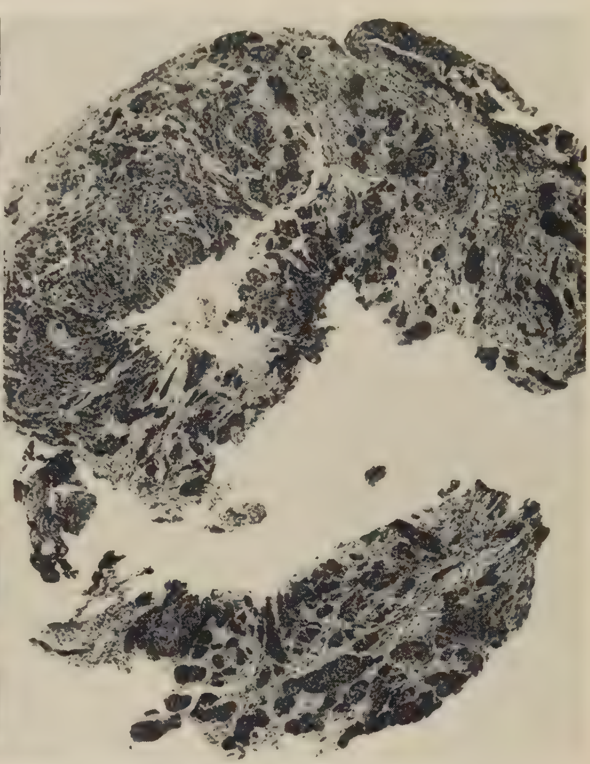

Middle Cranial Fossa
Middle Ear
Sup. Div. of Vestib. N.
Macula of Utricle

Acute myelogenous leukemia, initially manifest in temporal bone of 50 year old man with headache, tinnitus and bilateral deafness of rather sudden onset. Mucosa of middle ear is greatly thickened by leukemic deposits; labyrinth and internal auditory canal are practically filled with leukemic cells. Diagnosis made by biopsy. x8. Macula of the utricle is greatly thickened by leukemic infiltrations. x62. (S.R. Guild.)

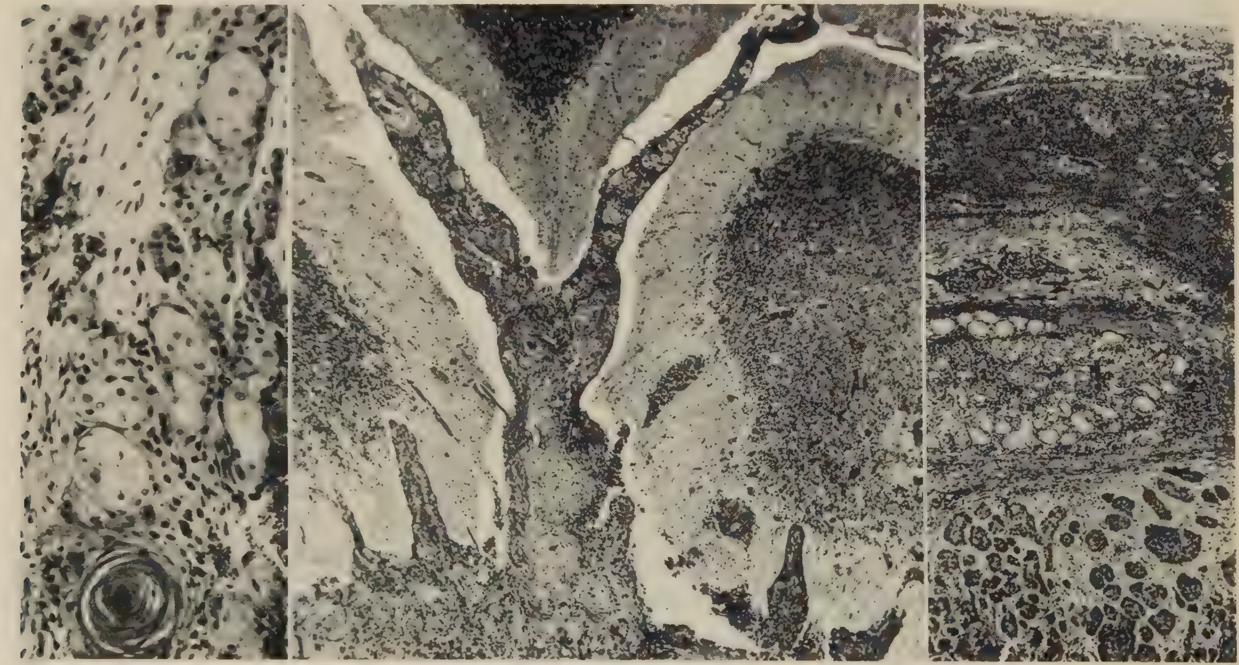
EPIDERMOID CARCINOMA, MIDDLE EAR



Carcinoma, primary in middle ear mucosa, projects into and fills tympanic cavity. Preserved mucosal surface at right. Specimen from radical mastoidectomy of 55 year old man with headache, intermittent earache, and draining ear. x48.

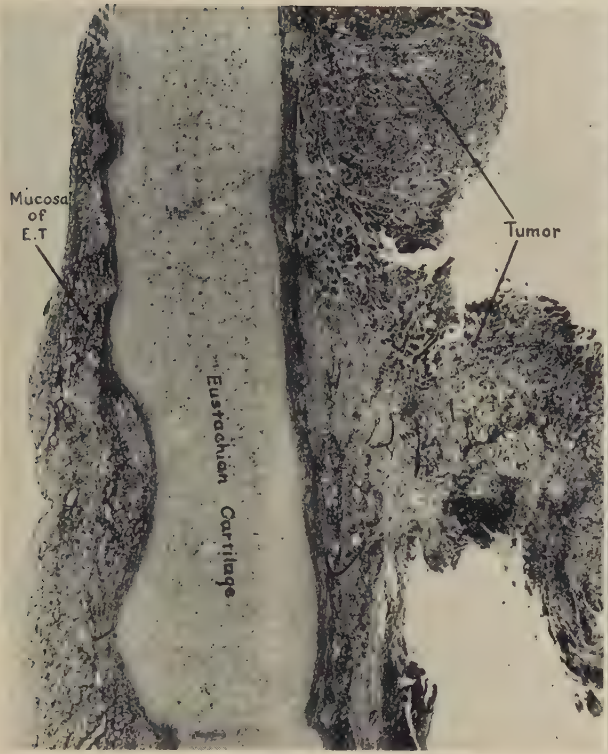


Local extension to mastoid, same case. Molded contents of a mastoid cell, removed at same operation, shows invasion by sheets and cords of neoplastic cells. x48. No tumor found in examination of the nasopharynx.

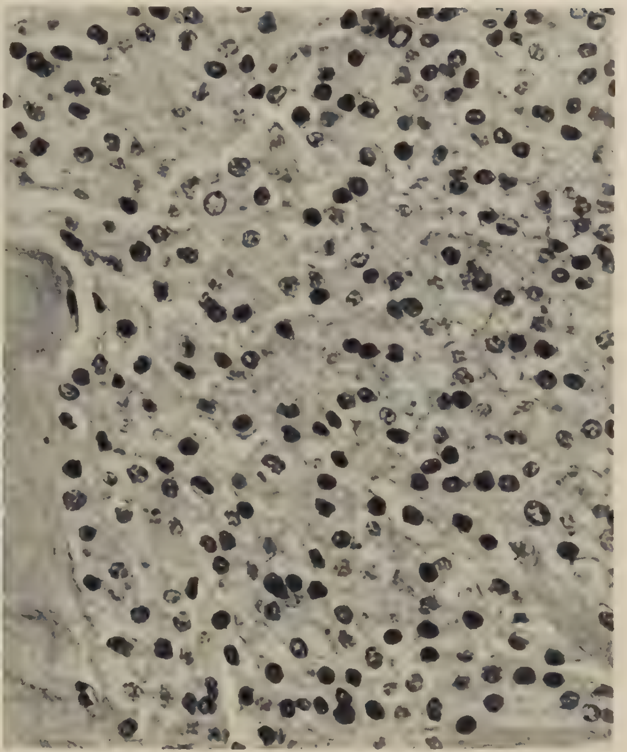


Direct intracranial extension. Invasion of meninges and cerebellum *(center)*, demonstrated at autopsy. x48. *Left:* detail of primary tumor *above*, surgically removed, includes an epithelial pearl. x125. *Right:* extension downward along eustachian tube (see following plate) to nasopharyngeal wall. Intact mucosa and lymphoid tissue of nasopharynx with small nests of tumor apparently within lymphatics at top; invading mass at bottom. x48. No distant metastases. (K.F. Ernst, Wash., D.C.)

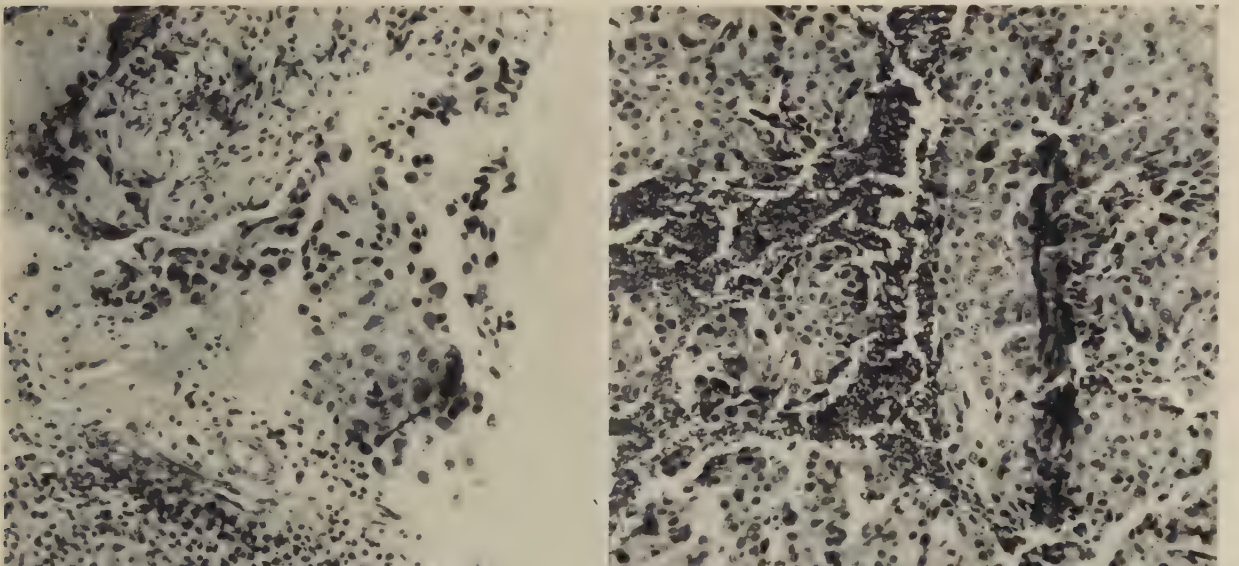
EPIDERMOID CARCINOMA, MIDDLE EAR AND MASTOID



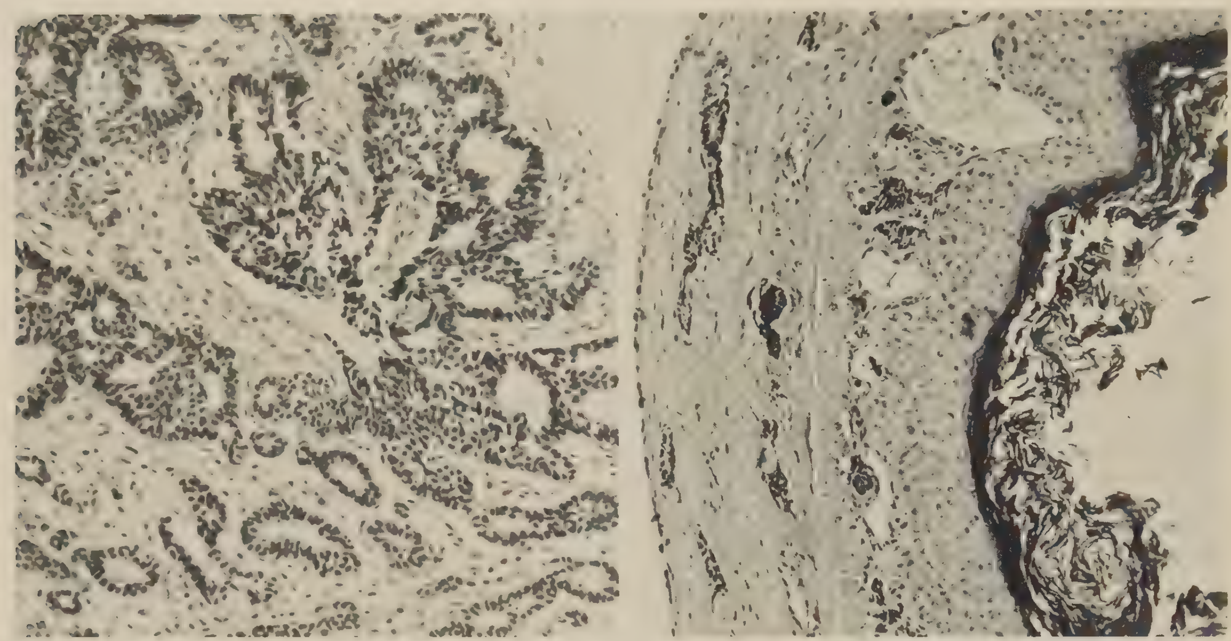
Extension to nasopharyngeal wall (from primary of preceding plate), almost to its mucosal surface at lower right, along eustachian tube. x13. More commonly, nasopharyngeal carcinoma extends to temporal bone with varying degrees of involvement.



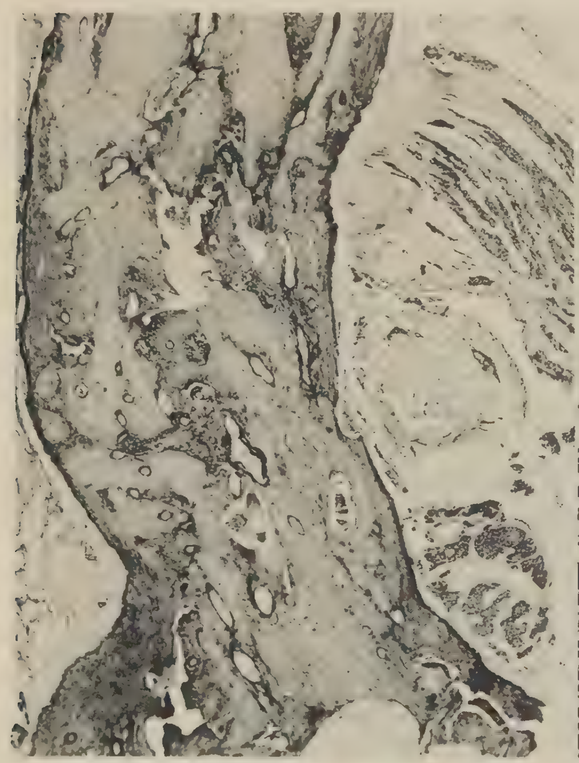
Metastatic undifferentiated carcinoma in mastoid, diagnosed as carcinoma arising in mastoid mucosa on initial biopsy. x400. Later, the maxillary sinus was found filled with tumor, and was considered the possible primary site.



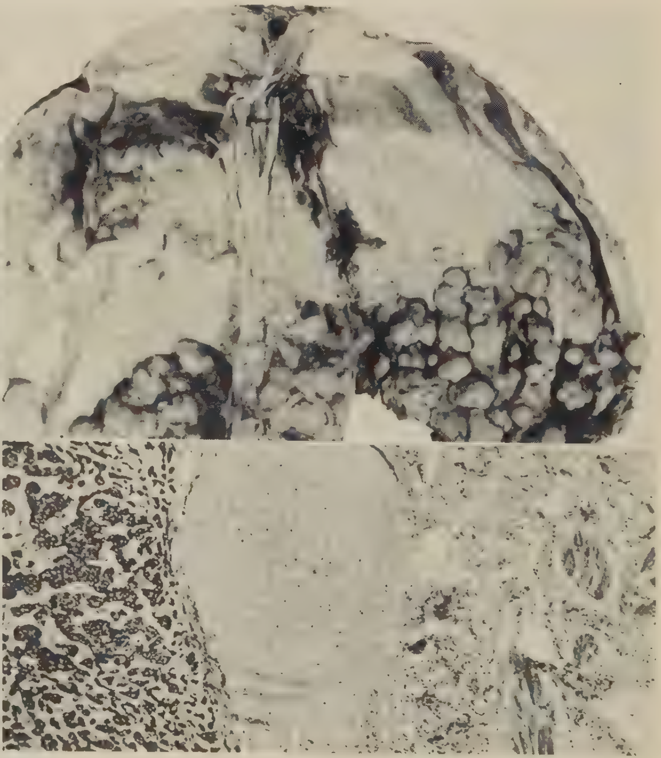
Presentation in external auditory canal, after filling middle ear, of a carcinoma primary in the epitympanum and involving mastoid cells. *Left:* biopsy of granulomatous mass in external auditory canal revealed several nests of well differentiated epidermoid carcinoma and small clusters of malignant cells. x185. *Right:* recurrent tumor in middle ear six months after radical mastoidectomy. x125. No nasopharyngeal carcinoma.



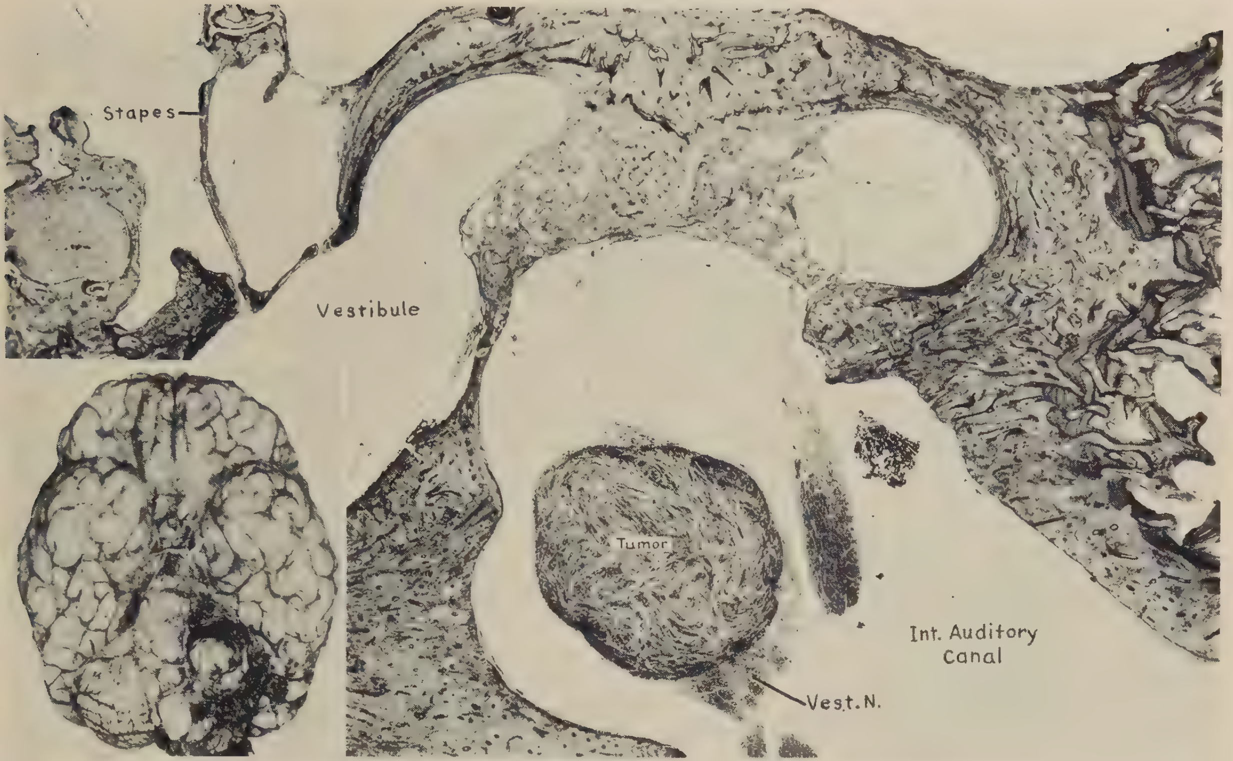
Adenocarcinoma (adenoid cystic), primary in epitympanic region in a 27 year old man, whose first symptoms were left facial paralysis and head pain, two years prior to death. Cerebellopontine angle tumor suspected. *Left:* contents of mastoid cell removed at radical mastoidectomy, at which time extensive tumor was noted. x185. *Right:* nests of tumor in lymphatic plexus of the tympanic membrane. External squamous epithelium markedly thickened and keratotic. Middle ear surface to left. Dilated vessels were noted clinically. x125.



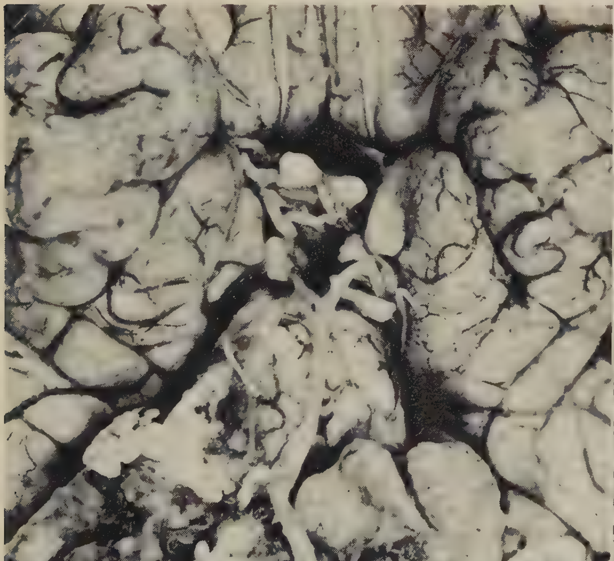
Extension to anterior portion of middle ear with involvement of facial nerve noted at same operation. *Above:* nests of tumor in and about maleus. x48. Previous adenoidectomy and nasopharyngeal biopsies negative for tumor; no other primary tumor.



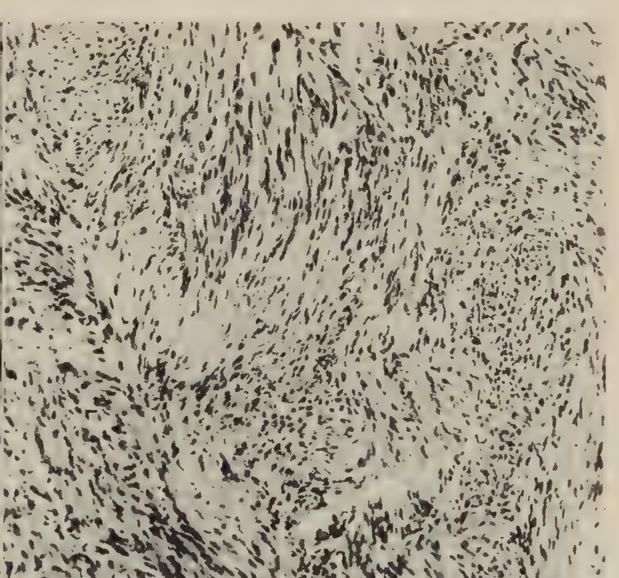
Metastases to lungs, pleura, liver, dura, meninges and bone, at autopsy. *Upper:* the stripped dura with extensive nodular subdural masses of tumor. *Lower:* circumscribed lung metastasis at left; bronchial cartilage in center; bronchial mucosa at right. x48.



Acoustic nerve tumor. Very small, round, encapsulated tumor which has arisen deep within the internal auditory canal; and, as is most common, on the vestibular nerve (its inferior branch in this case). Solid mass, but larger tumors often contain soft, cystic areas (E.K. Fowler, Jr.). *Inset:* large left cerebellopontine angle tumor, 4 cm. in diameter, in a 34 year old man, which compressed and displaced pons and medulla to right and distorted fourth ventricle.

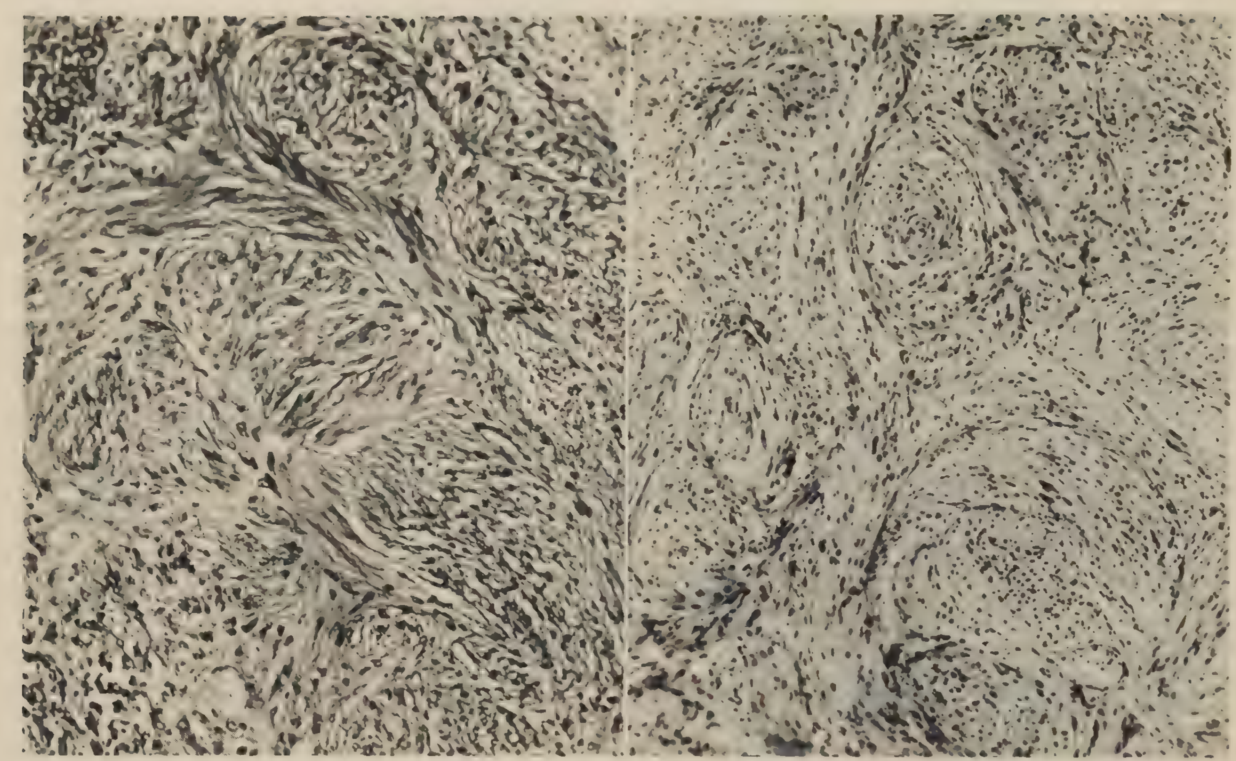


Bilateral acoustic tumors in a 24 year old man with multiple meningiomas and generalized neurofibromatosis. Right eighth nerve tumor partly removed six months before death.

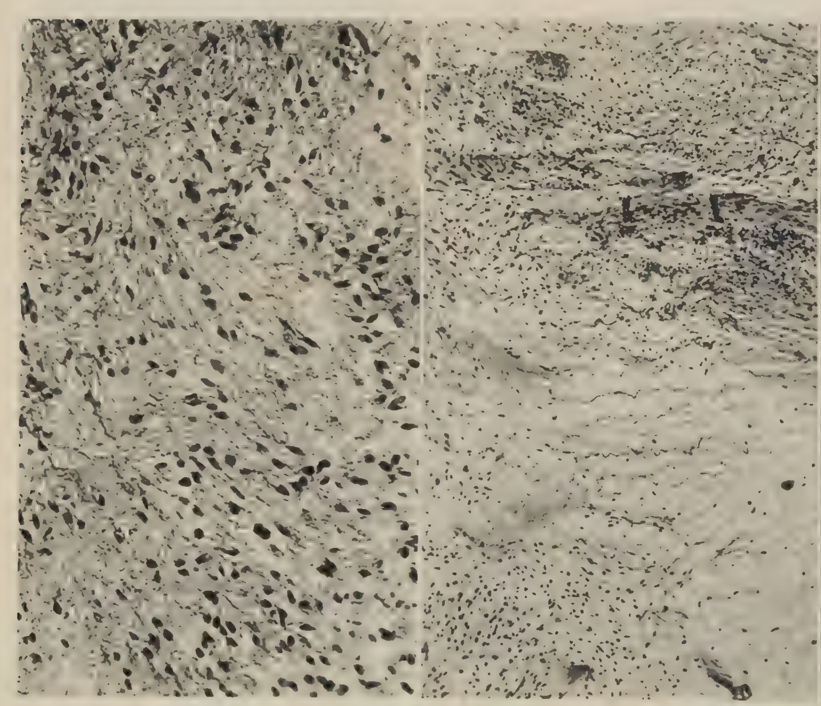


Cytologic structure. Solid (Antoni A) areas composed of intertwining bundles of fibers with palisading of nuclei and zones with nucleus-free parallel fibers. x125.

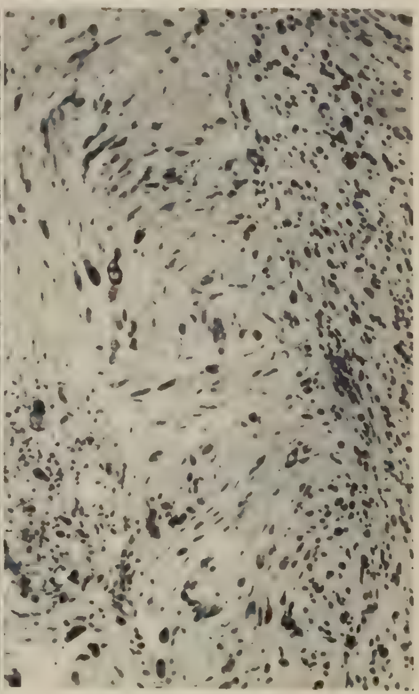
STRUCTURAL FEATURES



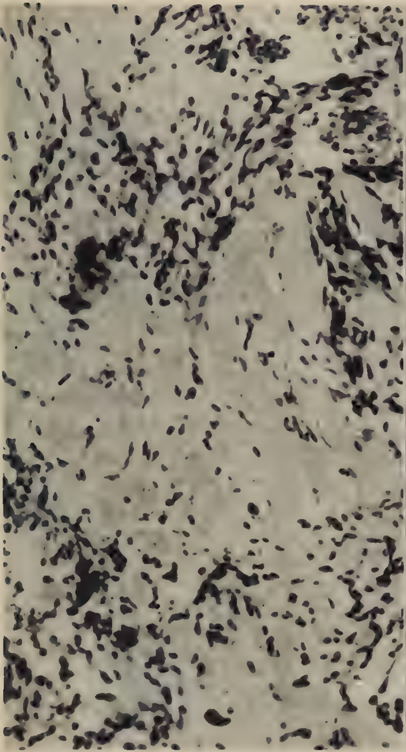
Antoni type A tissue. *Left:* solid interwoven bands of fibers and nuclei. Only suggestive alignment of nuclei. x165. *Right:* discrete whorled elements may suggest and sometimes mimic structure of tactile corpuscles—Verocay bodies. These fields are from bilateral case of preceding plate. x165.



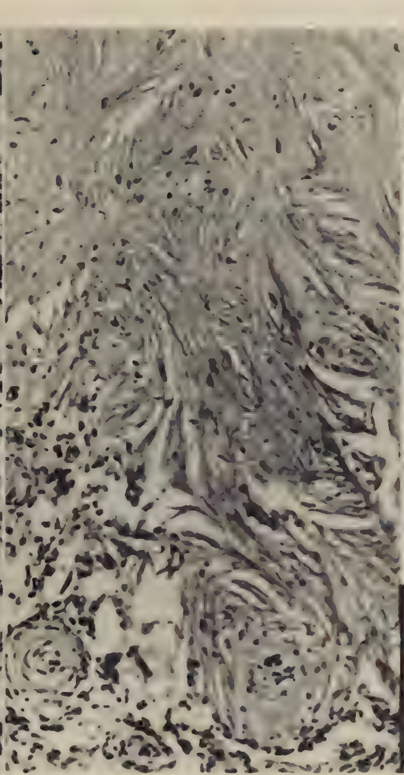
Antoni type B tissue. *Left:* finely fibrillar, less cellular area without interlacing pattern. x165. *Center:* very loosely fibrillar stroma; relatively acellular foci; areas of microcystic ("serous") degeneration, which fuse to form the larger interstitial cysts. x48.



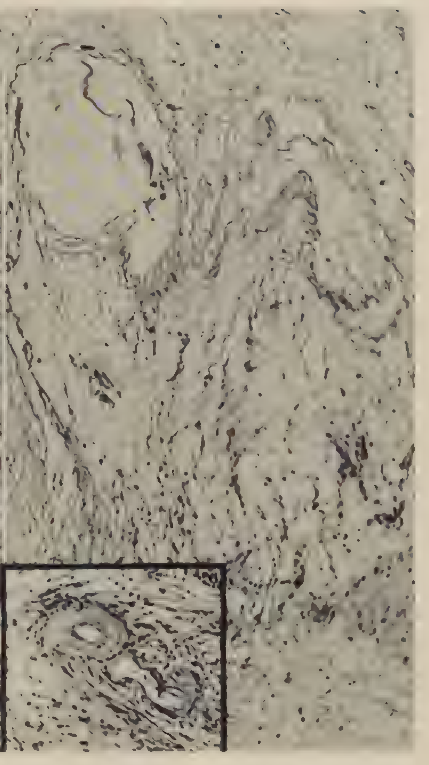
Bizarre degenerating cells vary in size and shape; have blurred, homogeneous chromatin content; show no mitotic activity. x125.



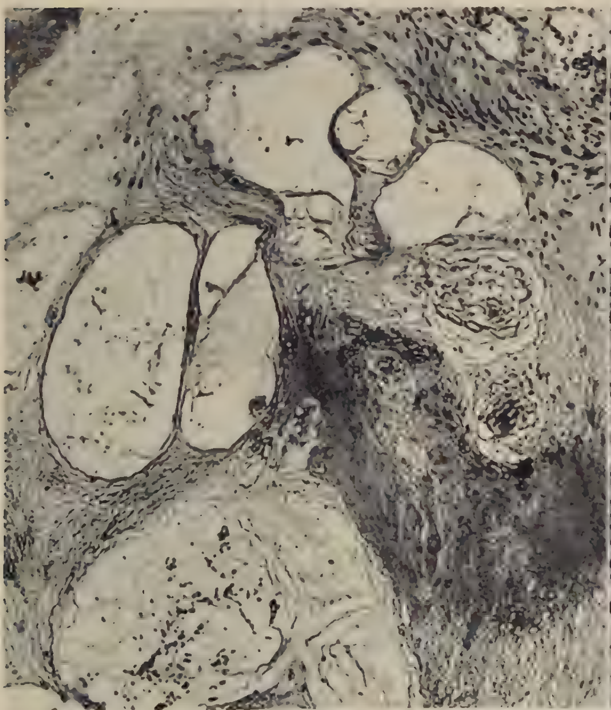
Hyalinizing bundles of nucleus-free fibers forming organoid structures. x145.



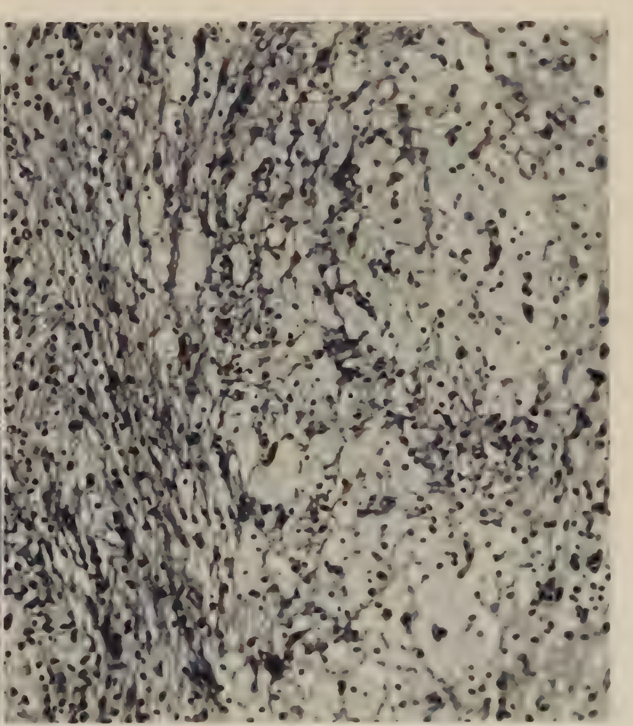
Densely collagenized areas, which stain like mesenchymal collagen, may be small or extensive. x125.



Small interstitial cysts in Antoni B tissue. x76. *Inset:* characteristic hyaline thickening of vessels. x48.



Formation of large cysts by fusion of microcystic spaces results in spongy or cystic gross structure. Believed to be the result of a serous type of degeneration. x75.



Lipid-laden foamy cells occur more frequently than in most peripheral neurofibromas. Considered histiocytes by some; degenerating tumor cells by others. x125.

CHAPTER 36

OTOSCLEROSIS, DEAFNESS AND MÉNIÈRE'S DISEASE

For a comprehensive appreciation of the historic aspects of otosclerosis and for orientation in the newer developments in the subject, the student should read the publications of the American Otological Society, Inc., the first of which is a resumé of the literature to 1935, edited by Fowler and Duel, and the second, a report of progress, covering the period 1926 to 1946. The classical monographs on the subject are those of Mayer and Wittmaack which are superbly illustrated.

The labyrinth is surrounded by dense bone which arises from the cartilaginous capsule and ordinary lamellar bone which arises from the mucoperiosteum of the middle ear. The middle layer of the labyrinthine capsule, which is the enchondral layer, differs from the rest of the skeleton by remaining in a more or less immature state, evidenced by the presence of cartilaginous remnants. This bone is further characterized by the absence of the normal haversian system.

The pathologic changes in otosclerosis consist of lacunar absorption of the normal bone and replacement by a vascular, spongy, osteoid type of new bone, some of it of the callus type. Later the new bone becomes denser and less vascular. These changes affect the enchondral capsule as well. The process resembles somewhat that of fibrous dysplasia of bone.

Guild described the histologic differentiation between the active and quiescent areas of otosclerosis. In the former the foci are much more vascular, show some marrow spaces, and the new bone is more cellular. In the quiescent, the bone is more solid, less vascular, and osteoblastic activity is practically at a standstill. This would indicate that otosclerosis is not necessarily a continuing process. It may cease to be active before irreversible damage is done to hearing. It is frequently in this arrested state in routinely examined material.

Otosclerosis occurs only at the sites where there are vascularized spaces in the bone and where specific germinal tissue exists. The most common site is in the bone between the foramen ovale and the cochlea. This area which contains the fissula ante fenestram also contains areolar tissue, connective tissue, cartilage and bone. It is particularly evident near the anterior margin of the oval window. From this focus the process may extend down the basal turn of the cochlea and involve the edge of the round window, and on into the vestibular capsule including the posterior ampulla. When the foot plate of the stapes is affected, it may become enormously thickened and the process may extend up the crura. Changes in the other ossicles occur in rare instances, but there is a question as to whether specific otosclerosis develops in them. Foci of otosclerosis are frequently multiple and dissociated.

The condition is more common in the female than the male and it is rare in Negroes. It can begin in early life, and foci thought by some to be otosclerosis have been found in the labyrinths of young babies. An instance of its occurrence in a 9-year-old boy is included in the illustrations.

Trauma and the developmental and traumatic fissures that are present in the bony capsule may exert a causative influence and there seems to be little doubt that heredity plays an appreciable role. The cause is unknown and it is not necessarily a specific or single one. The condition may be simply an osteodystrophy based on conditions that cause disturbances in other bones, but differing from that in other bones because of the developmental and histologic peculiarities of the labyrinthine bony capsule. The condition is usually bilateral.

Nager describes the process as an initial localized lacunar resorption of old capsular bone and its replacement by immature weblike bone containing considerable intercellular substance which takes a dark blue hematoxylin stain. This in turn undergoes lacunar absorption and replacement by more weblike bone containing thin foci of fibrous tissue, and finally the replacement of this by lamellar bone. This combination of weblike, cement-like bone and lamellar bone gives to the otosclerotic foci the irregular mosaic pattern. The process advances either on a broad peripheral basis or in finger-like projections from the primary focus.

The process may be limited to very small foci or be an extensive, richly vascularized area. Nodules at times project into the cochlea from the surface of the promontory or from the rim of the internal meatus, and if sufficiently large, they may impinge on the 8th nerve.

Kelemen has reviewed the reports of histologically characteristic foci of otosclerosis in sites other than the bony capsule, in lower animals as well as in man; for example, in the petrous outside of the capsule, in the ossicles and in the tegmen. These are certainly foci of bony dystrophy, but whether they can be considered the specific otosclerotic process is not certain. There is no verified instance of otosclerosis in lower animals.

The process does not necessarily impair hearing. Bezold's syndrome, therefore, will not reveal bone change in all instances. This syndrome is a progressive deafness of conduction type with normal tympanic membrane, and with hereditary and familial history of deafness.

Guild, after his study of 81 temporal bones, emphasized the fact that the mere presence of otosclerosis does not necessarily imply an impairment of hearing, for hearing is affected only when there is bony ankylosis of the stapedial foot plate in the oval window. Since the anterior margin of the oval window is the most common site of the lesion it is evident that only in a small percentage of cases does it bridge the gap to the foot plate. Guild was unable to demonstrate any influence of otosclerosis on the cochlear apparatus. It is readily seen, therefore, that sclerotic areas in parts of the capsule that do not involve the stapes are not as a rule a basis of impaired hearing. Specimens have been described in which the lower turn of the cochlea has been involved. It is also evident that, conversely, impaired hearing is not necessarily a basis for determining the genetic influence on otosclerosis.

The ineffectiveness of any measures to retard or stop the progress of the otosclerotic change has been overcome materially by the development of the fenestration operation. A report of the results in a large group of cases has been made by Lempert.

DEAFNESS

Developmental defects may result in complete or partial deafness. These extend through a wide range of possibilities that include one or more of the anatomic elements from the external ear to the neural elements of the labyrinths. If there is serious malformation of the external ear, anomalies of the internal structures can usually be anticipated, especially if the auditory canal is occluded. This, however, is not invariably so. Even with bilateral congenital atresia of the external ear, some hearing may be retained. In this circumstance the maldevelopments are more apt to be of the bony structures. Inherited congenital defects, most frequently of the cochlea, result in multiple instances of deafness in families.

The temporal bone illustrated is from an 11-year-old boy who was born totally deaf and who had had otorrhea for several years preceding his death from purulent meningitis. The structural defects are seen in the changes in the organ of Corti and in the tectorial membrane. In addition, there is obvious chronic suppurative inflammation involving the middle ear and the petrous portion of the temporal bone. The infection eroded through the cortex and into the meninges, causing the fatal illness.

Shambaugh and his coworkers made a statistical study of some 5,000 deaf children, in 3,300 of whom it was estimated that deafness was inherited. The statistics seem to emphasize the danger of consanguinity among those who have hereditary traits. Childhood diseases such as measles, scarlet fever, whooping cough, and meningitis and otitis media are among the commonest causes in the acquired cases.

Organization of intracranial birth hemorrhages into the inner ear will do irreversible damage. Maternal infections in the early months of pregnancy may have a serious effect on the ear. German measles has been incriminated, but congenital syphilis remains the most important of the intrauterine infections in this respect. An example of deafness from congenital syphilis is included in the illustrations. This material was from a 20-year-old man whose father had died of a ruptured aneurysm at 35. The patient exhibited other stigmata of congenital syphilis: keratitis, extensive scarring in the nasopharynx; and an active infection of the skull was found post mortem. His hearing was only slightly impaired at birth, but when he reached the age of 10 the infection became fulminant and he rapidly became deaf. Necrosis of the bone was extensive, hyperplastic inflammation of the middle ear had caused matting of the ossicles, the bony labyrinth was involved by a hyperplastic osteomyelitis which had invaded also the membranous labyrinth, and the aquaeductus endolymphaticus was almost occluded.

Inner Ear Deafness.—The well correlated study of Crowe, Guild and Polvogt on the pathology of high-tone deafness leads to the conclusion that arterio- and atherosclerosis are not causes of damage to the organ of Corti. However, with advanced arteriosclerosis, partial atrophy of the nerve to the basal coil is a common finding. A gradual rather than an abrupt impairment of hearing is characteristic of these patients. The authors concluded that inability to hear 4096 d.v. when low tones are well heard indicates extensive damage of the organ of Corti in the basal coil of the cochlea.

Streptomycin.—The clinical evidence of damage by streptomycin is incontrovertible, but the anatomic evidence in man is not well defined. It was supposed that because of the prominence of vertigo and deafness that damage to the membranous labyrinth would be obvious, but this has not been the case so far as the material available at AFIP is concerned. The chief histologic feature noted in several instances of tuberculous meningitis treated with streptomycin has been an inflammatory reaction in the meninges of the 8th nerve, but this was interpreted as a residuum of the meningitis. The specific lesion in man is obscured by the widespread tuberculous changes in the leptomeninges, cranial nerves, and sometimes in the bone and brain. Experimental work on normal animals has given a more accurate index of the pathologic changes caused by streptomycin. These results, however, are by no means uniform. Rüedi and his associates, working with guinea pigs, noted distinct changes in the ganglion cells and nuclei of the 8th nerve. More recently the experimental work of Caussé on mice and Berg on cats has shown that the effect of streptomycin is selectively on the epithelium of the crista of the vestibular organ. Rüedi and his co-workers have since confirmed these observations. Continuing research may give a definite answer.

Ménière's Syndrome (Hydrops of the Labyrinth). —There is considerable controversy, first, as to just what this syndrome is and, second, as to whether it is not a manifestation of a number of anatomic conditions. This is partially due to misinterpretation of Ménière's original reports. His first was simply a clinical description of a case of vertigo, nausea, tinnitus and deafness, and his next, thirteen years later, of somewhat similar symptoms in a case in which the autopsy revealed bloody exudate in the semicircular canals. The clinical picture was not at all that of his original case. We have, therefore, no real correlation between the pathology and the clinical syndrome attributable to Ménière. As pointed out by Williams, however, there is no question but that Ménière first described the disease that bears his name and established the fact that vertigo can originate in the ear.

Hallpike and Cairns, and more recently Lindsay, and Altmann and Fowler have established rather conclusively that hydrops of the endolymph system is at least a pathologic entity and that in some cases it is associated with the Ménière syndrome. It is still true, however, that tinnitus, vertigo, and deafness can be produced by other lesions of the ear and of the brain stem and by a blocked eustachian tube, but these are not to be included in the Ménière disease group. A fluctuating type of deafness has been added to the clinical syndrome. The syndrome is rarely seen in patients less than 30 years of age.

In spite of the apparent validity of the interpretation of the anatomic changes, the cause of them, and the physiologic relation between them and the clinical symptoms are still not clear. Williams has attempted to establish the disorder as a manifestation of physical or intrinsic allergy.

There is extreme dilatation of the cochlear duct and saccule causing herniations of the former through the helicotrema and of the utricle into the common crus, and Reissner's membrane is bowed. Other anatomic changes are lacking, except for extensive degeneration of the hair cells, and this can well be postmortem change. There is no evidence of an inflammatory factor. The details can be seen in the illustrations furnished by Lindsay.

The same pathologic changes have been found in cases where there was deafness but not the vertigo of the complete Ménière's syndrome. Lindsay accounts for this by assuming that the vertigo is an early symptom which may disappear in the later stages.

The auditory disturbances appear to be due to the mechanical interference with sound transmission in the column of fluid in the cochlea, and the vertigo to be based on the occurrence of the herniations into the canals from the utricle, producing distortion of the walls of the ampullae.

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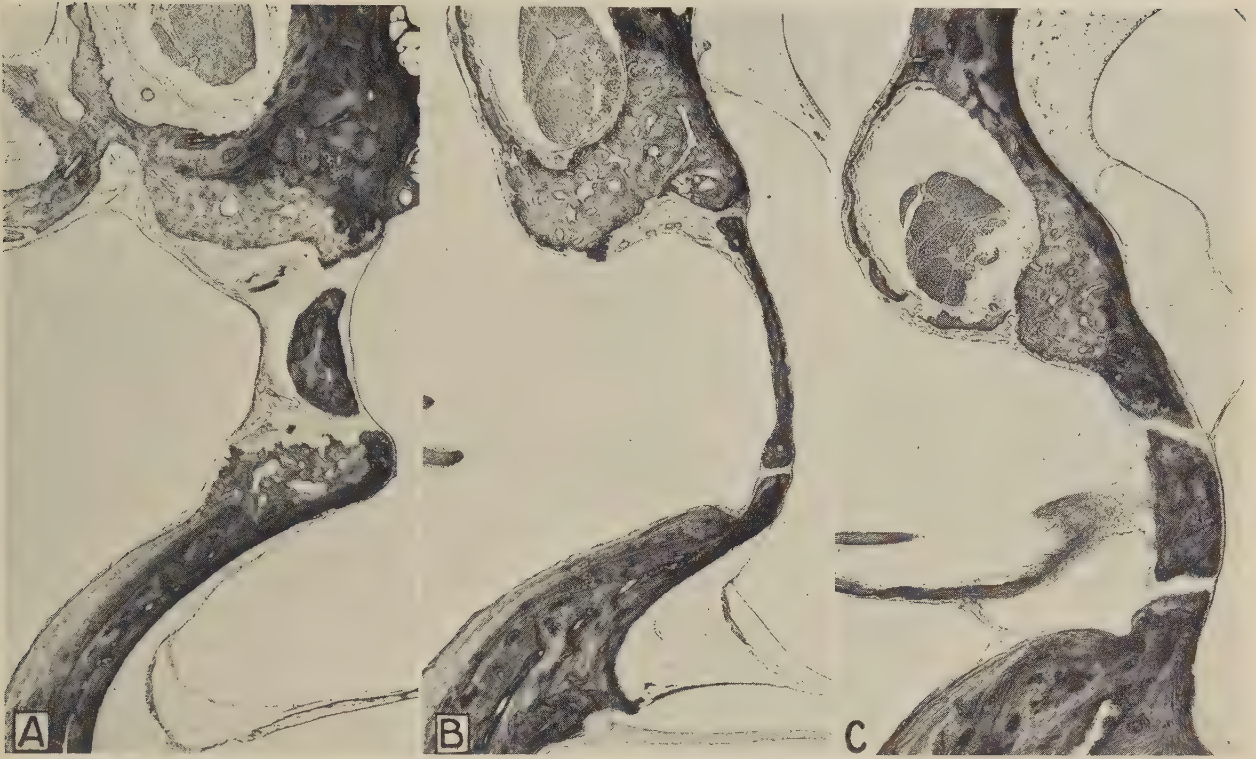
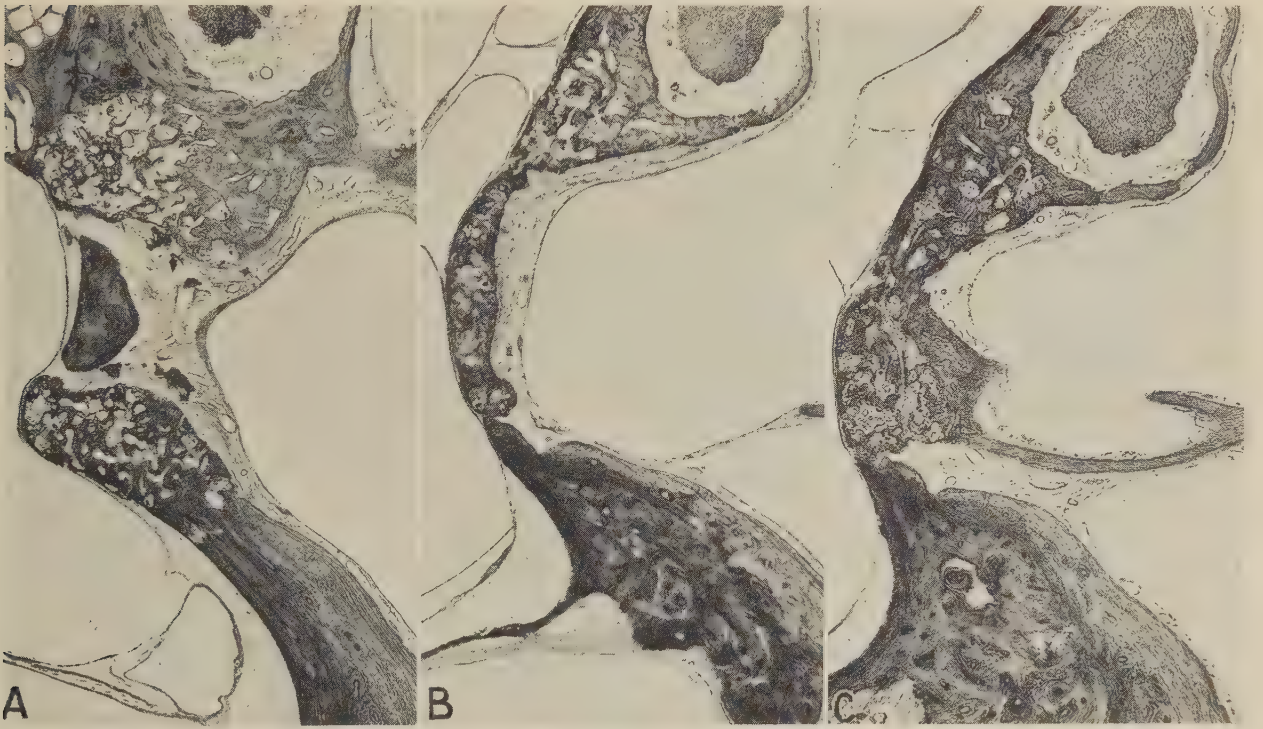
OTOSCLEROSIS

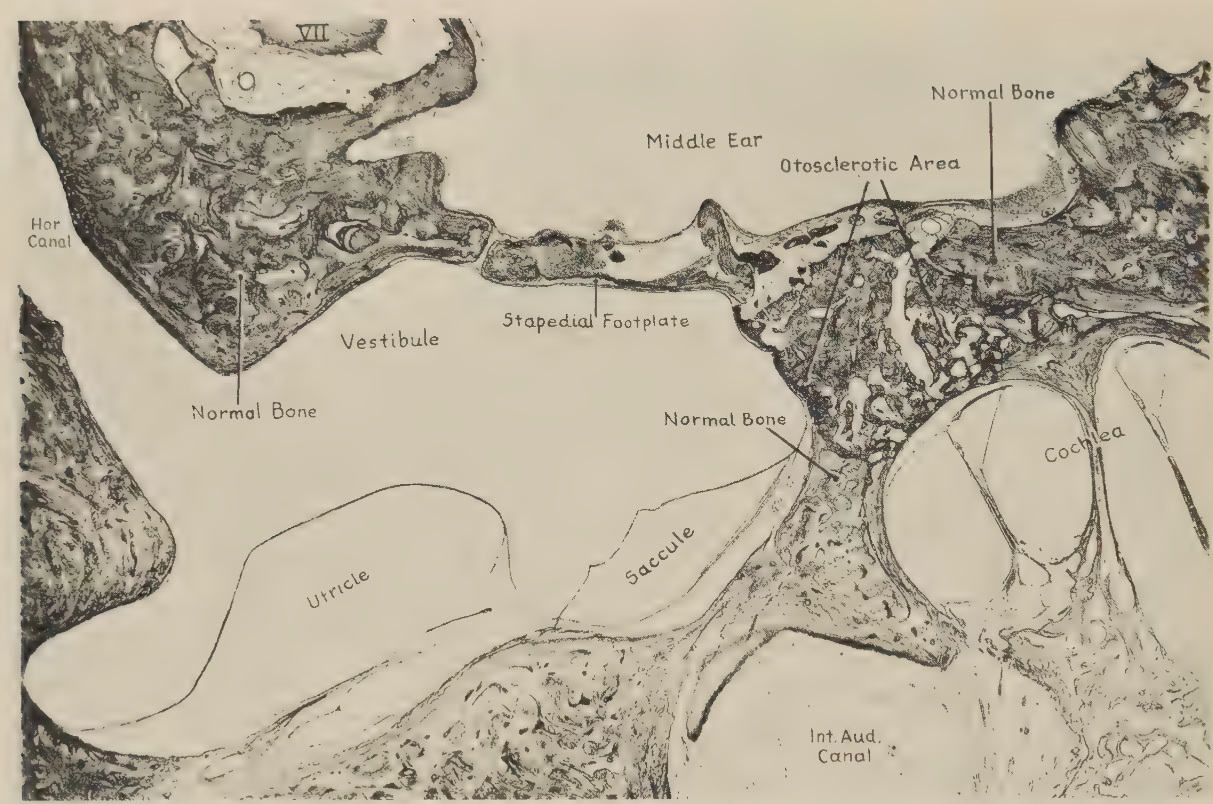
(OTOSPONGIOSIS; OSTEITIS VASCULOSA; ETC.)



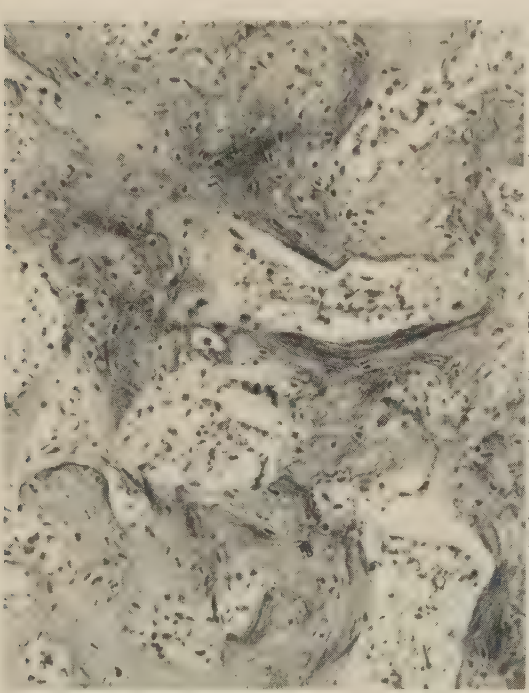
Right temporal bone. Vertical sections through anterior **(A)**, middle **(B)**, and posterior **(C)** thirds of the oval window. Otosclerotic area in bony labyrinthine capsule is quiescent; the annular ligament is intact; and there is no ankylosis of the stapes. Middle ear mucosa at left is normal. (S.R. Guild.)



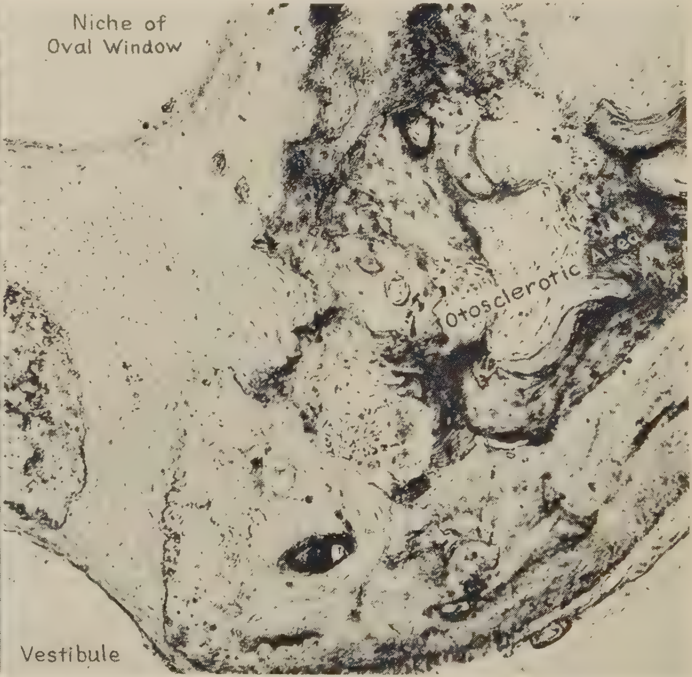
Left temporal bone of same patient. Vertical section through corresponding areas of the oval window of the left ear. Active otosclerosis involving superior and inferior margins of window **(A)** and footplate of stapes, which is ankylosed **(B and C).** (S.R. Guild.)


VII
Hor Canal
Normal Bone
Middle Ear
Otosclerotic Area
Normal Bone
Stapedial Footplate
Vestibule
Normal Bone
Normal Bone
Cochlea
Utricle
Saccule
Int. Aud. Canal

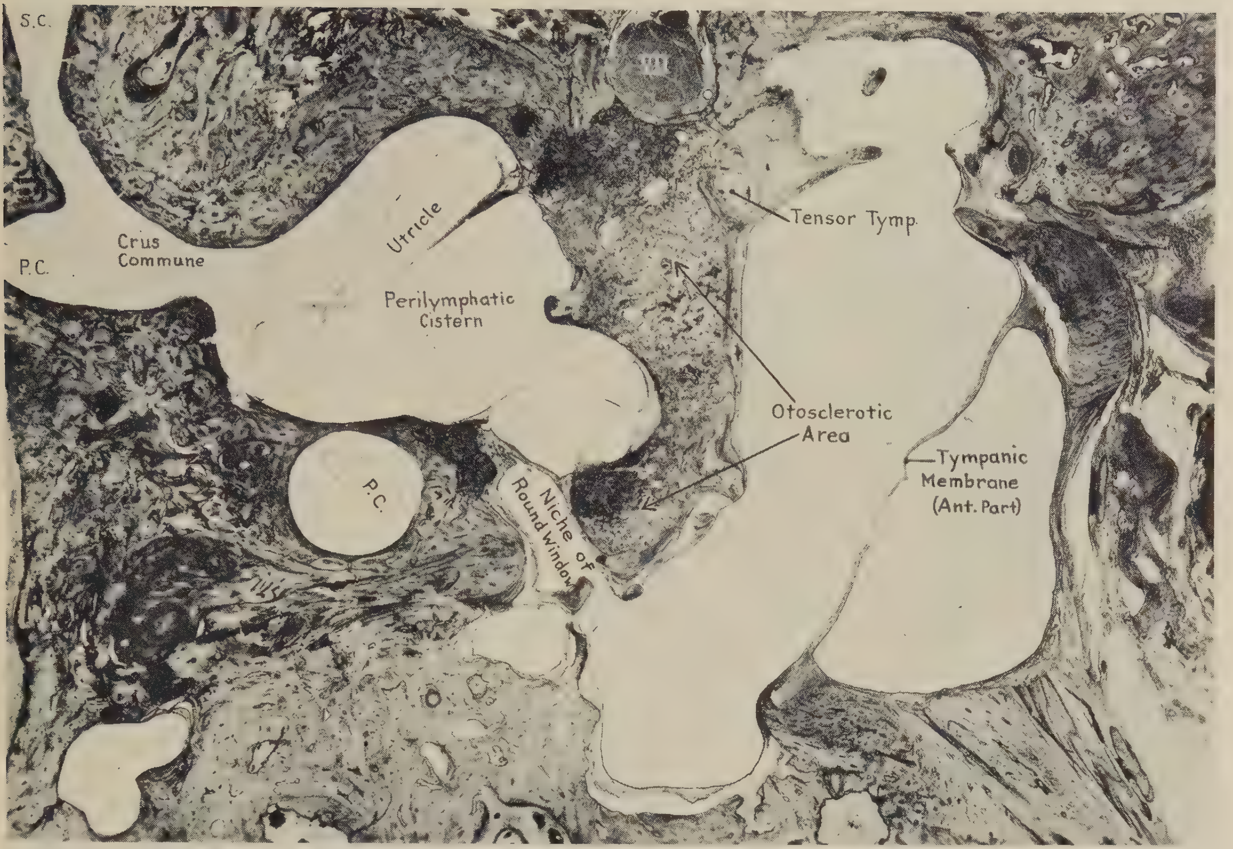
"Area of predilection." Otosclerotic area anterior to oval window extending through entire thickness of bony labyrinthine capsule between cochlea and vestibule. Ankylosis of stapes at this point. Note large vascular spaces within the "otoclerotic" bone. Horizontal section of left temporal bone. x15. (S.R. Guild.)



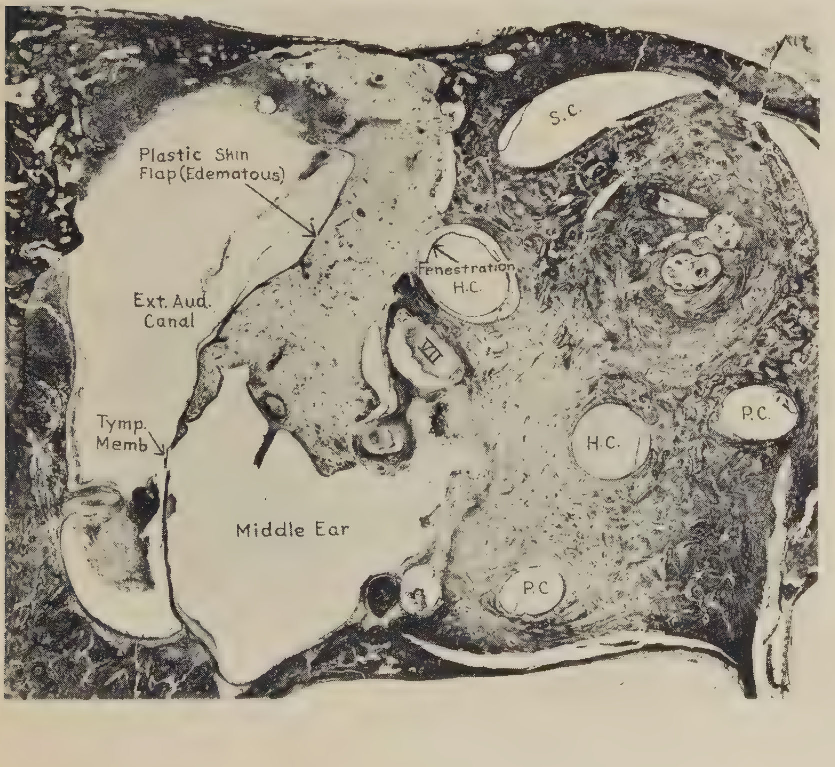
Otosclerotic ("blue") bone. Vascular fibrous tissue and irregular bone trabeculae (blue in H & E stain). Older, denser, regularly laminated foci take red stain ("red bone"). (E.P. Fowler, Jr.)


Niche of Oval Window
Otosclerotic Area
Vestibule

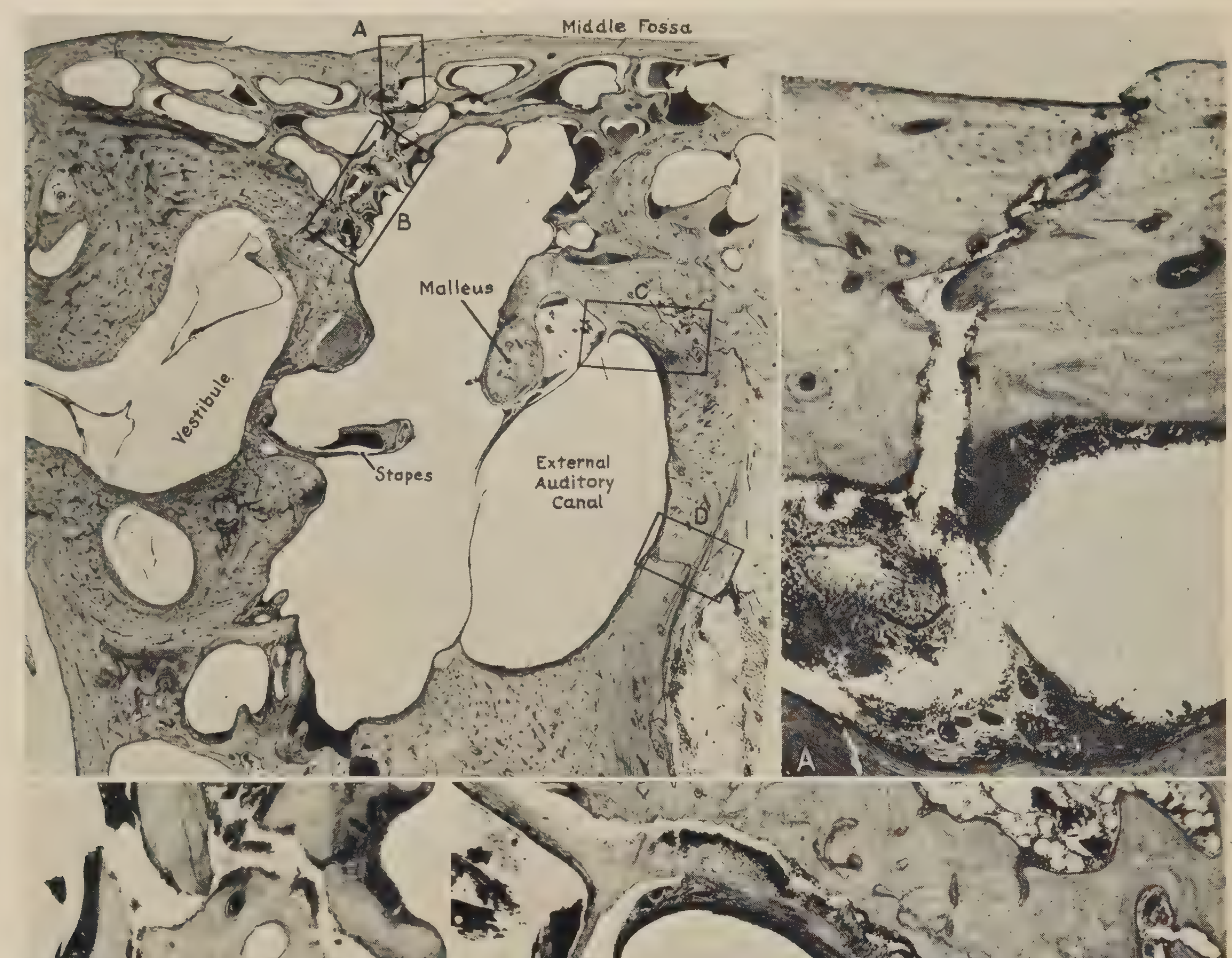
Active foci in anterior margin of oval window. There is fibrosis of annular ligament at left, but no ankylosis of stapes. Otosclerosis in a 9 year old child who died of brain tumor. No deafness. (J.R. Lindsay, Chicago.)


S.C.
P.C.
Crus Commune
Utricle
Perilymphatic Cistern
Tensor Tymp.
Otosclerotic Area
Tympanic Membrane (Ant. Part)
P.C.
Niche of Round Window

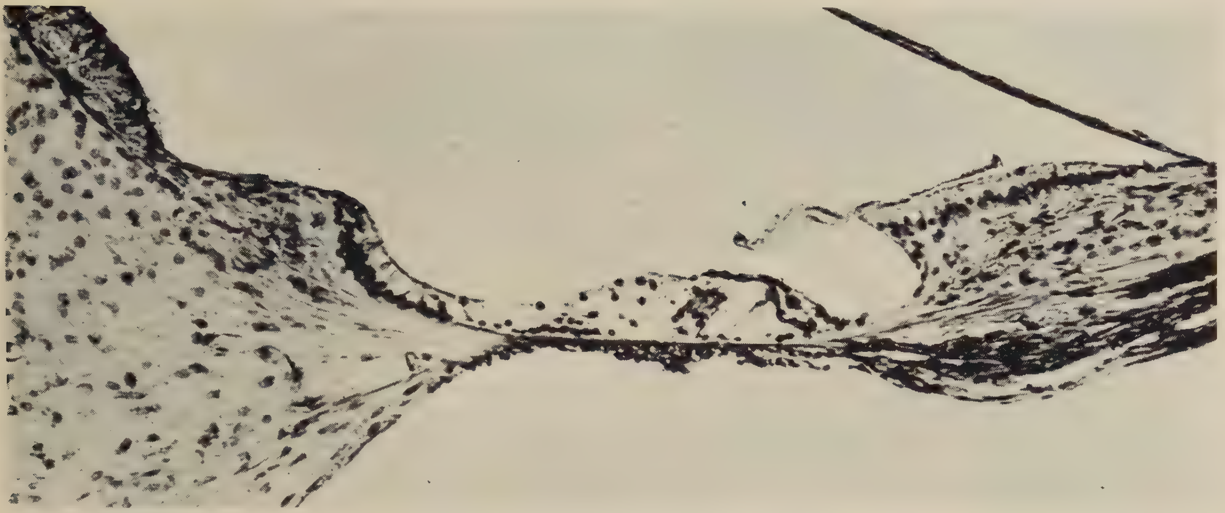
Advanced otosclerosis has completely filled and blocked oval window and involved footplate of stapes. The round window is narrowed by otosclerotic foci at both margins. Bone conduction in this patient was greatly reduced. (E.P. Fowler, Jr.)


S.C.
Plastic Skin Flap (Edematous)
Fenestration H.C.
Ext. Aud. Canal
VII
P.C.
H.C.
Tymp. Memb
Middle Ear
P.C

Autopsy specimen after fenestration operation. 50 year old patient with bilateral progressive deafness died of coronary disease sixteen days after operation. The fenestration of the labyrinth was made from the anterior part of the ampullated end of the horizontal canal over the ampulla itself *(arrows)*. The bony defect is neatly filled and covered by the tympanomeatal flap, that is continuous with the freed upper margin of the tympanic membrane. The flap is very edematous, and an edematous prolongation of its stroma hangs down in the middle ear cavity. There is no evidence of regenerating bone in the smooth margins of the fenestration. **H.C.,** horizontal semicircular canal; **S.C.,** superior semicircular canal; **P.C.,** posterior semicircular canal. (Case of D.G. Woodman, New York, courtesy of E.P. Fowler, Jr.)

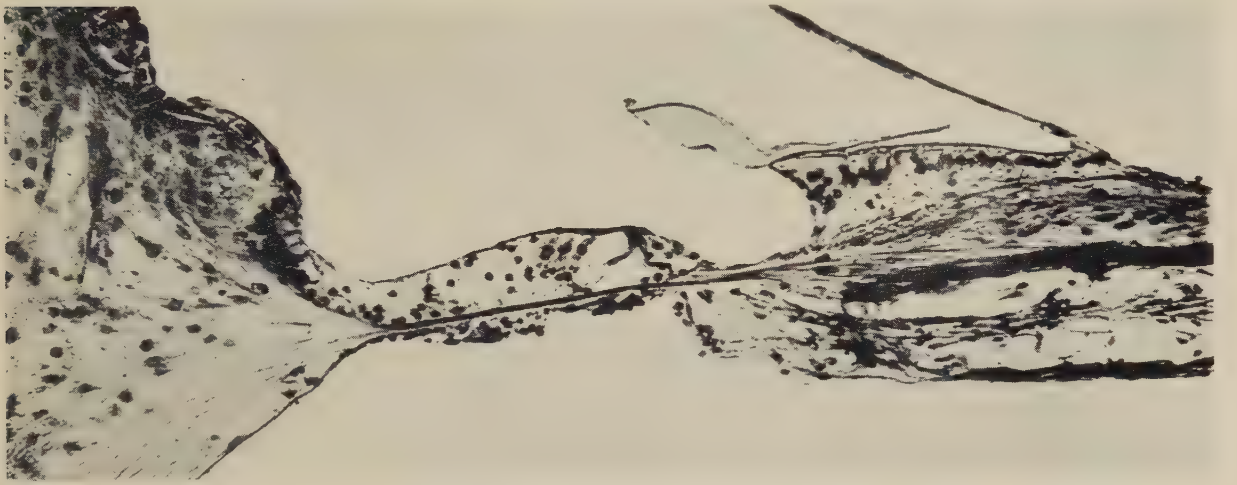

A
Middle Fossa
B
Malleus
C
Vestibule
Stapes
External
Auditory
Canal
D
A
B
C
D

Longitudinal fracture through tegmen tympani (A) extends through trabeculated bone in medial wall of attic **(B),** and laterally to the bony wall of the external auditory canal (**C** and **D**). Hemorrhage into the middle ear (hematotympanum) and rupture of the tympanic membrane, as in this case, occur frequently in this type of fracture, which results in a conduction type of deafness because of involvement only of middle ear and tympanic membrane. Transverse fractures primarily involve the inner ear; are less common, but more serious; result in complete nerve deafness, if the patient survives. (E.P. Fowler, Jr.)



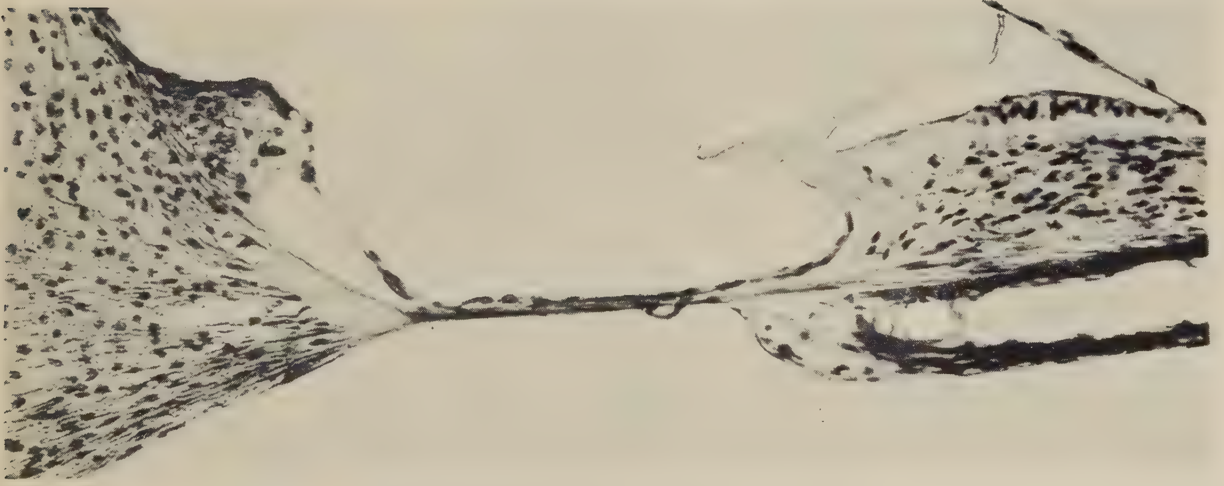
Normal Organ of Corti; Normal Nerve.

In the basal turn of the cochlea, where receptors for high tones are located.



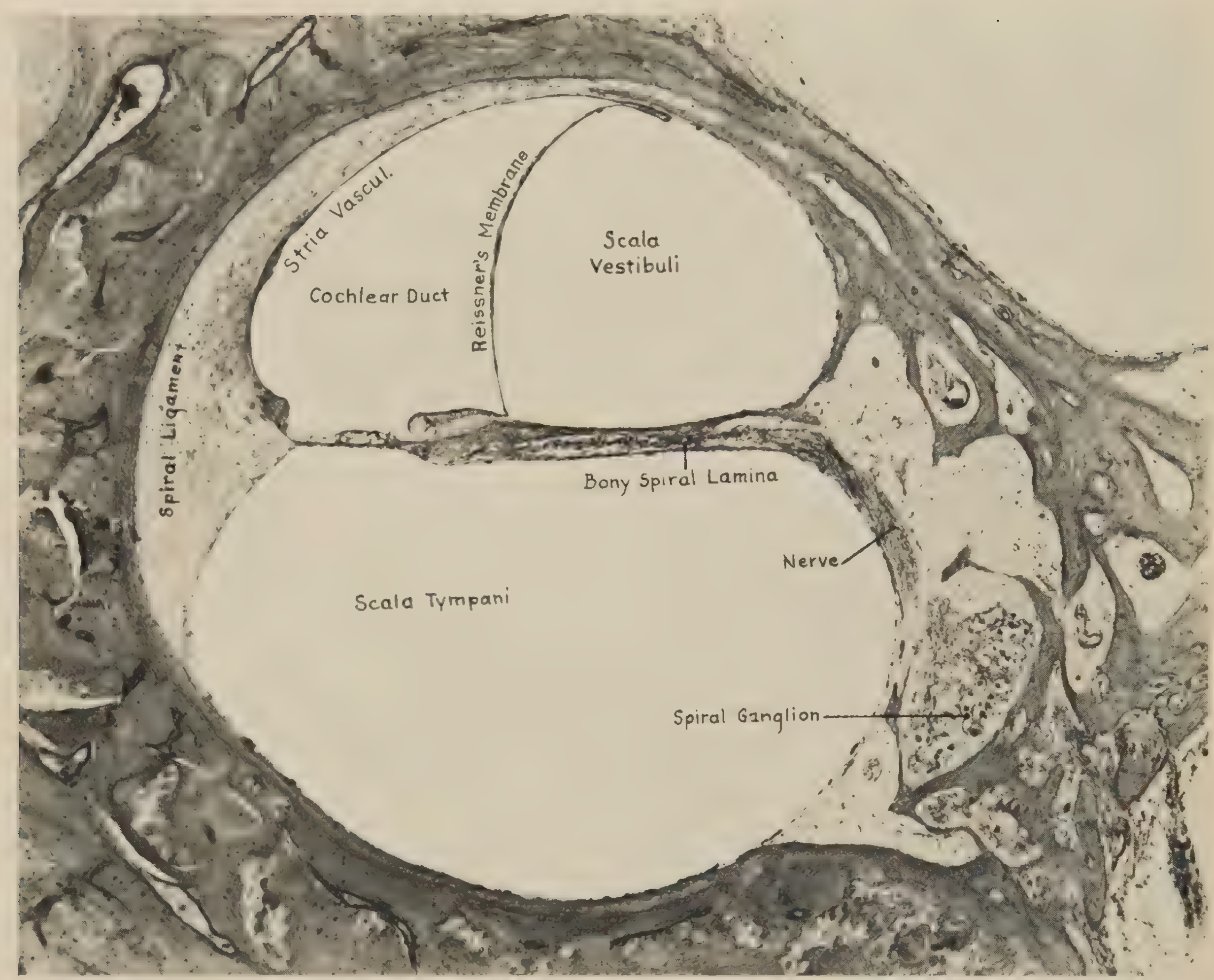
Normal Organ of Corti; Partial Atrophy of Nerve.

Typical lesion in gradual "high tone loss."

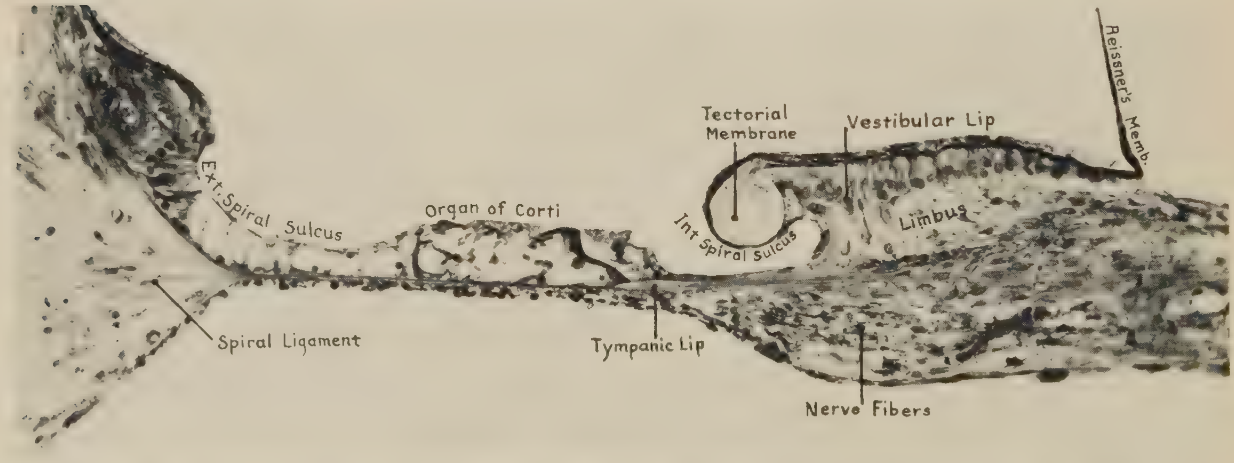


Complete Atrophy of Organ of Corti and of Nerve.

(All from S.R. Guild.)


Stria Vascul.
Reissner's Membrane
Scala Vestibuli
Cochlear Duct
Spiral Ligament
Bony Spiral Lamina
Nerve
Scala Tympani
Spiral Ganglion

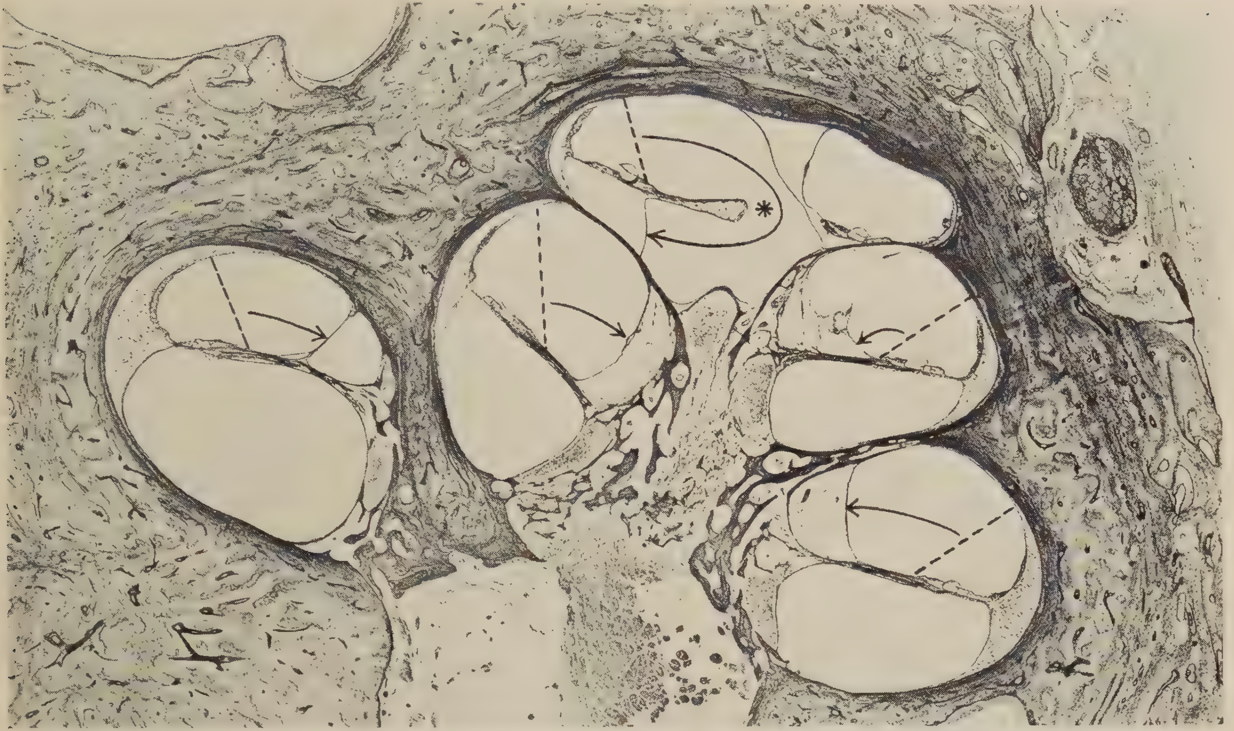
Congenital deafness. Section from basal coil of cochlea. Reissner's membrane (vestibular membrane) extends vertically upward to the outer bony wall forming a 90° angle, instead of a normal angle of 45° with the basilar membrane. This has resulted in a greatly enlarged cochlear duct and a small scala vestibuli. The stria vascularis is poorly developed. x60. A boy born deaf, in subsequent years had otorrhea, pain and tenderness in left ear. Death from meningitis at eleven years of age.


Reissner's Memb.
Tectorial Membrane
Vestibular Lip
Ext. Spiral Sulcus
Organ of Corti
Int. Spiral Sulcus
Limbus
Spiral Ligament
Tympanic Lip
Nerve Fibers

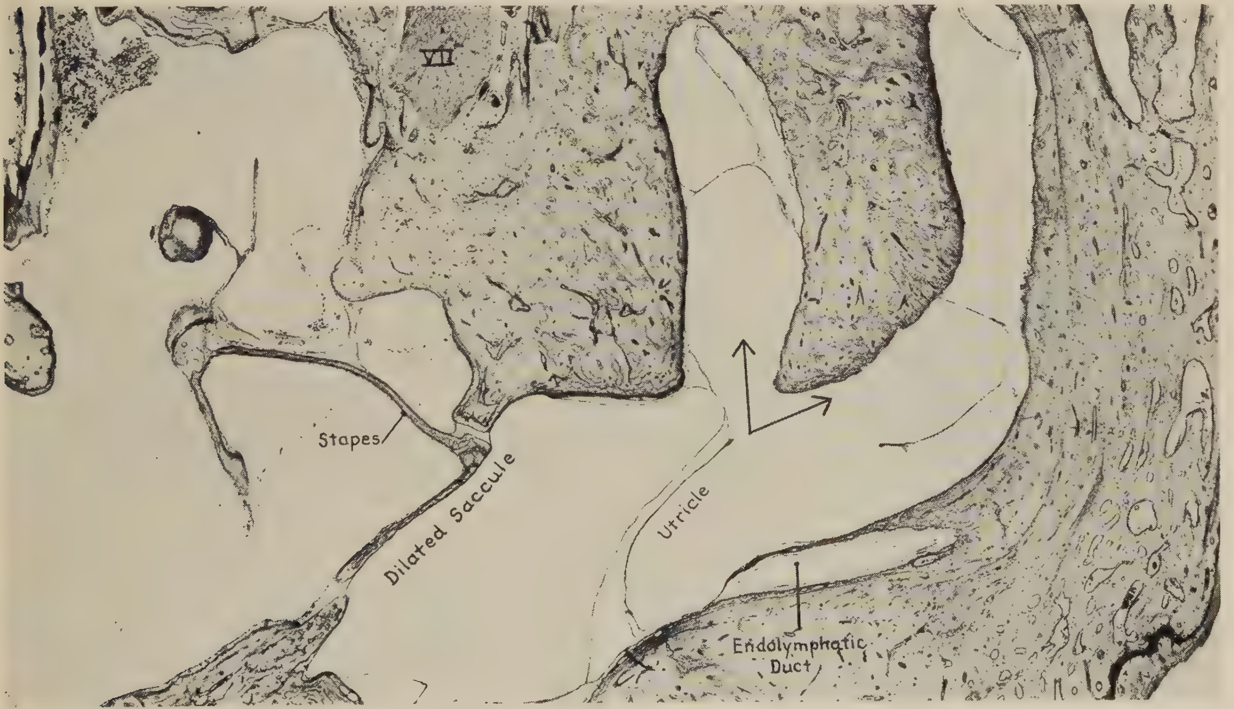
Magnified field showing organ of Corti, poorly formed; tectorial membrane enclosed by epithelium and rolled up into internal spiral sulcus. x300.
It is possible that such changes resulted from intrauterine inflammation. (D.P. Cordray, Mosher Laboratory, Boston.)

MÉNIÈRE'S DISEASE

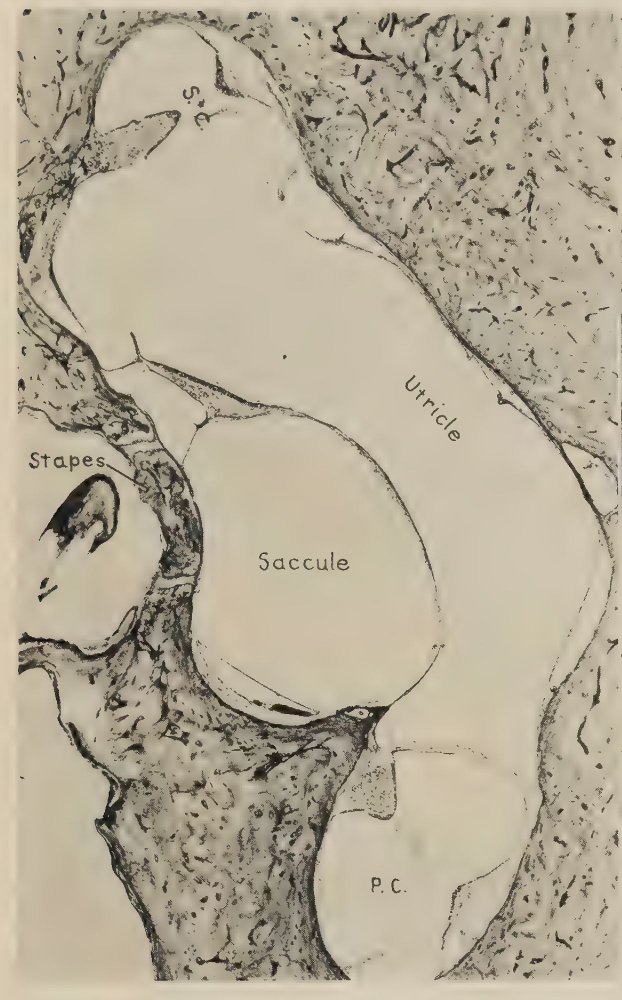
IDIOPATHIC HYDROPS OF THE ENDOLYMPHATIC SYSTEM



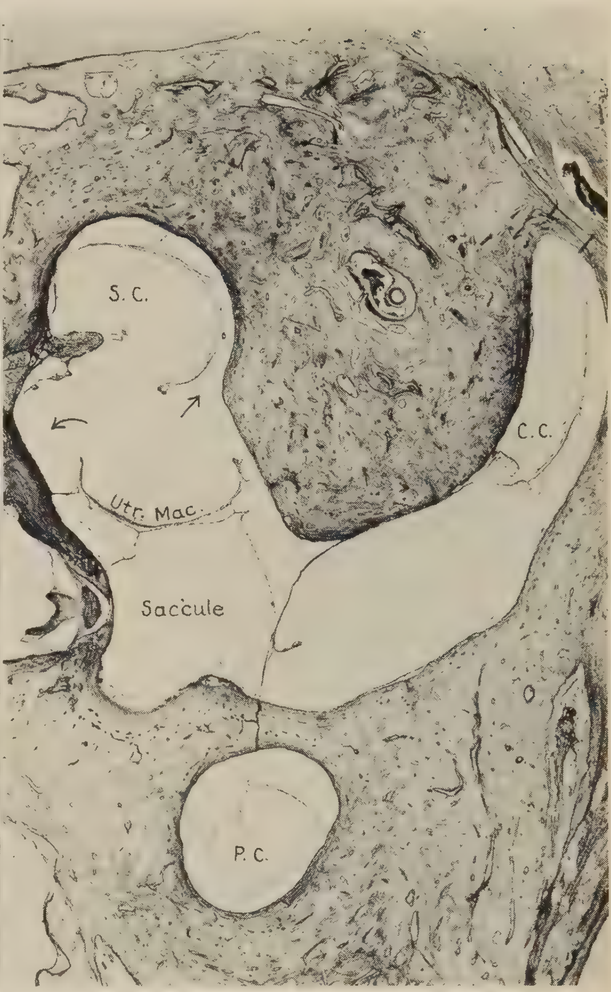
Marked dilatation of the cochlear duct, a constant finding in "idiopathic labyrinthine hydrops." Vertical section through cochlea of a man with Ménière's syndrome for fifteen years. In the apical turn, extremely dilated cochlear duct has herniated through the helicotrema into the scala tympani. In all, the scala vestibuli is almost obliterated. *Arrows* point to "ballooned out" Reissner's membrane; *dotted lines* indicate its normal position.



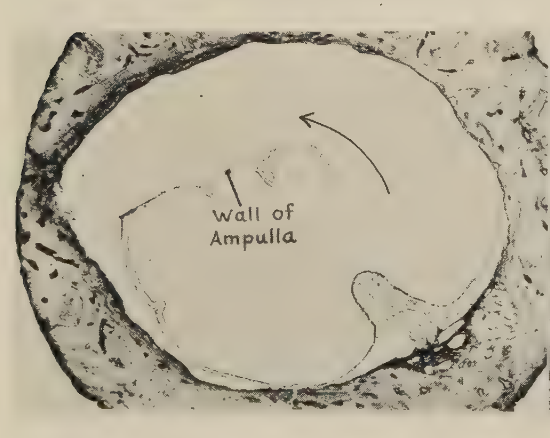
Dilated saccule and utricle in horizontal section through vestibule of another case of idiopathic labyrinthine "dropsy." The saccule, normally small at this level, is enormously dilated; covers the inner surface of the stapedial footplate; fills the perilymphatic cistern. The walls of the utricle have herniated into the perilymphatic space of the small end of the horizontal canal and the common crus *(arrows)*. (Both from J. R. Lindsay.)



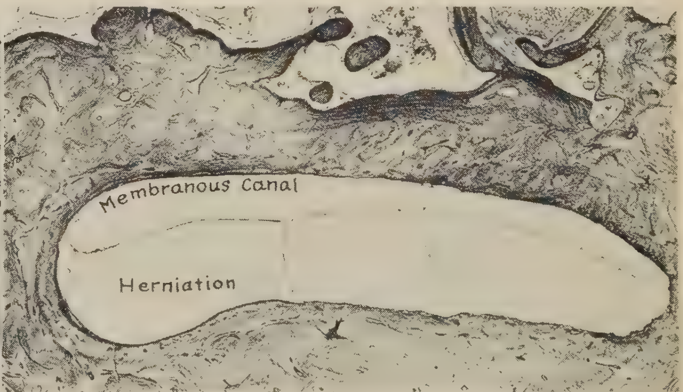
Vertical section through vestibule with hydrops. Dilated saccule is in contact with footplate of stapes. Greatly dilated utricle shows distortion and herniation at junction with posterior canal ampulla **(PC)** and with ampulla of superior canal **(SC).**



Vertical section at posterior border of vestibule of same case. Extremity of dilated saccule and edge of utricular macula on left. Dilated utricle shows small herniation at ampulla of superior canal *(arrows)* and a diffuse dilatation filling end of crus commune.



Ampulla of posterior canal with herniation of utricle *(arrow)* between the bone and the wall of the ampulla.



Posterior canal beyond ampulla with herniation of utricle, that has extended through the ampulla and completely fills the perilymphatic space.

Figures from A.A.O.&O. Home Study Course Manual on Ménière's Disease by J.R. Lindsay.

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